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COMPARISON OF THE CARBON DIOXID TENSION OF THE ALVEOLAR AIR AND THE HYDROGEN-ION CONCENTRATION OF THE URINE WITH THE BICARBONATE OF THE BLOOD PLASMA *

OSCAR M. SCHLOSS, M.D., AND HELEN HARRINGTON, M.A.
NEW YORK BALTIMORE

During the past two years data have been obtained from normal infants and from infants suffering from acidosis which permit a comparison of the carbon dioxid tension of the alveolar air, and the acidity of the urine with the plasma bicarbonate.[1]

TECHNIC

Alveolar air was collected by the Plesch-Higgins method as modified by Howland and Marriott. A large number of the analyses were made by the Haldane apparatus, the remainder by the colorimetric method of Marriott.[2] We have found the latter method to be quite accurate when carefully used and the results vary but little from those obtained by the Haldane apparatus. It seemed evident that any errors inherent in the colorimetric method were less than those associated with the method of collection of the alveolar air.

The plasma bicarbonate was determined by the method of Van Slyke and Cullen;[3] corrections for temperature and barometric pressure were made from their table.

Hydrogen-ion concentration of the urine was determined by the method of Henderson and Palmer.[4]

When the alveolar air and the plasma bicarbonate were compared, the alveolar air was collected first and the blood withdrawn within a few minutes. When crying occurred during the air collection the infant was quieted and kept so for a few minutes before the blood was taken. The blood was withdrawn from the superior longitudinal sinus by means of a syringe, care being

* Read before the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

* From the Children's Wards, Bellevue Hospital, Dr. L. E. La Fétra, Director, and the Pathological Laboratory, Bellevue Hospital, Dr. Douglas Symmers, Acting Director. This work was aided by a grant from the Rockefeller Institute for Medical Research.

1. All cases of acidosis considered in this paper were of the variety due to gastro-enteric disorders.

2. Marriott, J. McK.: J. A. M. A. **66**:1594, 1916.

3. Van Slyke, D. D., and Cullen, G. E.: J. Biol. Chem. **30**:289, 1917, their table.

4. Henderson, L. J., and Palmer, W. W.: J. Biol. Chem. **17**:305, 1914.

taken to prevent the entrance of air. By means of a glass tube and rubber attachment applied directly to the syringe, the blood was transferred underneath a layer of mineral oil in a centrifuge tube, contact with the air thus being entirely avoided. By these precautions the values obtained were for venous blood and could therefore accurately be compared with the carbon dioxid tension of alveolar air collected by the Plesch-Higgins method.[5]

Comparison of the hydrogen-ion concentration of the urine and the plasma bicarbonate was effected as follows: The infant was placed on a metabolism frame and the urine collected for four hours. At the end of two hours, blood was withdrawn for the determination of the plasma bicarbonate.

COMPARISON OF PLASMA BICARBONATE WITH CARBON DIOXID TENSION OF ALVEOLAR AIR

Normal Infants. — The plasma bicarbonate of normal infants[6] ranged from 49 to 72 volumes per cent. of carbon dioxid bound as bicarbonate at 0° and 760 mm. barometric pressure. These values are lower than those for normal adults.[7] The carbon dioxid tension of alveolar air varied from 34 to 45 mm. of mercury. The carbon dioxid tension of alveolar air and the plasma bicarbonate of normal infants are shown in Table 1.

$$\frac{\text{The plasma bicarbonate } (Co_2, \text{ V. P. C.})}{Co_2 \text{ tension of alveolar air}}$$

ranges from 1.22 to 1.84 with an average value of 1.5. The factor by which the carbon dioxid of the plasma bound as bicarbonate must be multiplied to convert it into terms of carbon dioxid tension of alveolar air is $\frac{1}{1.5} = 0.66$. The close correspondence between the direct determination of the carbon dioxid tension of alveolar air and its calculation from the plasma bicarbonate is shown in Table 1. It is of considerable interest that the factors 1.5 and 0.66 are identical with those which apply to adults.[7] There has always been some question as to the accuracy of the collection of alveolar air from infants. The fact that the air is collected for a definite time, despite the rapidity and amplitude of respiration, suggests a possible source of error. Our results, however, indicate that in normal infants the collection of alveolar air by the Plesch-Higgins method as modified by Howland and Marriott gives an accurate index of the plasma bicarbonate.

Infants with Small Tidal Air Volume.—The accuracy of the collection of a sample of alveolar air from infants is dependent to some degree on the manner in which the infant breathes. This fact has been pointed out by Marriott. With a little experience one can tell almost exactly whether the air collection is satisfactory. In very small

5. This method gives the carbon dioxid tension of venous blood.

6. All of the patients on whom investigations were conducted were under 18 months of age.

7. Van Slyke, Stillman, and Cullen: J. Biol. Chem., **30**:401, 1917. Gettler and Baker, J. Biol. Chem. **25**:211, 1916.

infants whose tidal air volume is small, or sick infants with shallow respirations, the analysis of alveolar air may be very misleading. The results from a group of such infants are shown in Table 2.

TABLE 1.—Comparison of the Tension of Carbon Dioxid in Alveolar Air with the Plasma Bicarbonate in Normal Infants

Case No.	CO_2 Tension of Alveolar Air, Mm.	Plasma Bicarbonate. CO_2 Bound at 0° and 760 Mm., Volume per Cent.	Plasma Bicarbonate. Volume per Cent. of CO_2 Bound at 0° and 760 Mm. CO_2 Tension of Alveolar Air, Mm.	Plasma Bicarbonate. (Volume per Cent. CO_2) × 0.66 to Give CO_2 Tension of Alveolar Air, Mm.
1	38.0	61.7	1.62	40.7
2	35.0	52.1	1.49	33.9
3	37.5	52.1	1.39	34.4
4	34.0	59.5	1.75	39.2
5	34.0	49.8	1.46	32.9
6	37.0	55.6	1.50	36.8
7	40.0	49.0	1.22	32.4
8	45.0	71.0	1.58	46.8
9	38.0	54.0	1.42	35.6
10	39.0	59.7	1.61	39.4
11	38.0	52.2	1.37	33.9
12	32.5	51.8	1.60	34.2
13	38.0	59.7	1.57	39.4
14	40.0	61.3	1.53	40.5
15	41.5	60.4	1.45	39.9
16	39.8	61.9	1.55	40.9
17	36.3	51.2	1.41	33.9
18	44.1	73.2	1.65	48.2
19	40.6	60.0	1.48	39.6
20	39.0	71.7	1.84	47.3
21	43.2	58.6	1.38	38.6

It is quite evident that a consideration of carbon dioxid tension of alveolar air alone would have led to the diagnosis of acidosis, while the plasma bicarbonate showed that none existed. The reason for this error is obvious. The tidal air volume is so small that but little air enters the bag, most being taken up by the dead space in the mask. The air withdrawn from the bag for analysis contains a large proportion of atmospheric air. In practically every case shown in Table 2 it was realized at the time the test was made that the collection of alveolar air was unsatisfactory, and that the results would be too low.

TABLE 2.—Comparison of Tension of Carbon Dioxid in Alveolar Air with Plasma Bicarbonate in Infants with Shallow Respiration

Case No.	CO_2 Tension of Alveolar Air, Mm.	Plasma Bicarbonate. CO_2 Bound at 0° and 760 Mm., Volume per Cent.	Plasma Bicarbonate. (Volume per Cent. CO_2) × 0.66 to Give CO_2 Tension of Alveolar Air, Mm.	Difference Between Determined CO_2 Tension of Alveolar Air and CO_2 Tension of Alveolar Air Calculated from Plasma Bicarbonate
1	24	51.3	33.8	9.8
2	25	....	45.5	20.5
3	30	63.5	42.0	12.0
4	22	54.0	35.3	13.3
5	16	48.0	31.3	15.3
6	21	53.0	35.0	14.0
7	26	62.0	41.5	36.0
8	27	58.0	38.0	11.0
9	22	56.0	37.0	15.0

From these results it seems evident that the carbon dioxid tension of alveolar air and the plasma bicarbonate correspond closely only in infants whose tidal air is of moderate volume. In infants with shallow respirations, the alveolar air may lead to the diagnosis of acidosis when none exists. In such cases the plasma bicarbonate must be used as a guide or a mask devised which has a smaller dead space.

Infants Suffering from Acidosis.—The results from cases of acidosis are given in Table 3. They show a fairly close correspondence between the alveolar air and the plasma bicarbonate. This, however, is true only before the administration of sodium bicarbonate. In Table 4 is shown results from a group of infants who had been given a sufficient amount of sodium bicarbonate to restore the alkaline reserve. In many of the cases the alveolar air analysis showed results which were too low despite the correction of acidosis. It seems that the respiratory center may remain hyperirritable after the correction of acidosis. Whether this is a direct result of the disease, or whether the respiratory center is capable of stimulation by conditions other than an increased hydrogen-ion concentration of blood, remains to be determined.

COMPARISON OF THE HYDROGEN ION CONCENTRATION OF THE URINE AND THE PLASMA BICARBONATE

Effect of Food.—In Tables 5, 6 and 7 are shown the hydrogen-ion concentration of the urine (negative logarythm) and the plasma bicarbonate of apparently normal infants who were receiving different types of food. The hydrogen-ion concentration ranged from a maximum of

TABLE 3.—Comparison of Tension of Carbon Dioxid in Alveolar Air with Plasma Bicarbonate in Infants with Acidosis

Case No.	CO_2 Tension of Alveolar Air, Mm.	Plasma Bicarbonate. CO_2 Bound at 0° and 760 Mm., Volume per Cent.	Plasma Bicarbonate. (Volume per Cent. CO_2) × 0.66 to Give CO_2 Tension of Alveolar Air, Mm.	Difference Between Determined CO_2 Tension of Alveolar Air and CO_2 Tension of Alveolar Air Calculated from Plasma Bicarbonate
1	14	32.6	21.8	7.8
2	23	37.3	24.6	1.6
3	28	39.1	25.8	2.2
4	17	24.3	15.0	2.0
5	19	22.3	14.6	4.3
6	22	21.4	14.1	7.9
7	26	37.3	24.6	1.4
8	20	41.1	27.1	7.1
9	17	25.4	16.75	0.25
10	26	44.8	29.6	3.6
11	23	39.1	25.8	2.8
12	20	36.0	23.8	3.8
13	26	48.1	31.7	5.7
14	31	41.6	27.4	3.6
15	22	35.4	23.4	1.4
16	28	45.7	30.1	2.1
17	20	22.3	14.7	5.3
18	26	43.0	28.4	2.4
19	26	48.4	31.9	5.9
20	24	42.4	27.3	3.3
21	25	44.3	29.2	4.2
22	11	14.4	9.5	1.5
23	22	37.0	14.5	7.5
24	18	19.7	13.0	5.0
25	19	39.1	25.8	6.8
26	28	33.0	21.8	6.2
27	27	38.5	25.4	2.4
28	28	42.4	28.0	0.0
29	33	50.1	33.1	0.1
30	18	26.4	17.4	0.6
31	20	39.6	26.2	6.2
32	24	36.0	23.8	0.2
33	20	30.9	20.4	0.4

4.1 to a minimum of 6.9. The average hydrogen-ion concentration of the urine from all cases was 5.24. Henderson and Palmer found that the urine of adults showed an average hydrogen-ion concentration of 6. The hydrogen-ion concentration of the urine of infants closely corresponds to the lower carbon dioxid tension of alveolar air and the lower plasma bicarbonate.

TABLE 4.—Comparison of Carbon Dioxid Tension of Alveolar Air with Plasma Bicarbonate in Cases of Acidosis after Correction of the Acidosis

Case No.	CO_2 Tension of Alevolar Air, Mm.	Plasma Bicarbonate. CO_2 Bound at 0° and 760 Mm., Volume per Cent.	Plasma Bicarbonate. (Volume per Cent. CO_2) × 0.66 to Give CO_2 Tension of Alveolar Air, Mm.	Difference Between Determined CO_2 Tension of Alveolar Air and CO_2 Tension of Alveolar Air Calculated from Plasma Bicarbonate	Sodium Bicarbonate, Gm.
2 (a)	23	37.3	24.6	1.6	6.0 subcutaneously
(b)	29	55.0	36.1	7.1	
5 (a)	17	24.3	15.0	2.0	5.4 subcutaneously
(b)	23	57.2	37.1	14.1	
14 (a)	23	39.1	25.8	2.8	7.0 intravenously
(b)	37	60.3	39.8	2.8	
17 (a)	20	36.0	23.8	3.8	6.6 subcutaneously
(b)	28	72.0	47.5	19.5	
20 (a)	22	35.4	23.4	1.4	6.8 subcutaneously
(b)	29	68.7	45.3	16.3	
24 (a)	26	48.4	31.9	5.9	7.1 intravenously
(b)	32	58.6	38.6	6.6	
27 (a)	11	14.4	9.5	1.5	4.5 intravenously
(b)	20	70.8	46.6	20.6	
29 (a)	18	19.7	13.0	5.0	3.8 subcutaneously
(b)	24	80.6	53.0	29.0	
30 (a)	19	39.1	25.8	6.8	6.4 intravenously
(b)	25	78.8	52.0	27.0	

(a) = before administration of sodium bicarbonate; (b) = after administration of sodium bicarbonate.

Marriott suggests that the lower alveolar carbon dioxid in infants is due probably to more active metabolism, leading to the greater production of acids. Tables 5, 6 and 7 show that the hydrogen-ion concentration of the urine bears a definite relationship to the type of food. The urine was more acid in infants receiving food richer in protein. The tables of Gettler show that the ash of milk is very weak in bases and could therefore neutralize but little acid.[8]

The influence of food on the hydrogen-ion concentration of the urine is shown by the work of Blatherwick,[9] and this influence is what

8. Gettler, A. O.: Dissertation, Columbia University, 1912.
9. Blatherwick, N. R.: Arch. Int. Med. **14**:409, 1914.

might be expected from the base contents of the food. In a number of our cases, the direct influence of food was shown by dietetic experiment. The results from two infants are shown in Table 8. In both instances, the addition of potato, which has a markedly alkaline ash, caused a reduction in the acidity of the urine. In both cases a similar, though less marked, influence on the alkaline reserve was observed.

TABLE 5.—HYDROGEN-ION CONCENTRATION OF URINE AND PLASMA BICARBONATE OF INFANTS FED ON DILUTED COW'S MILK

Case No.	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Plasma at 0° and 760 Mm.	Case No.	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Plasma at 0° and 760 Mm.
1	5.7	54.3	9	4.8	57.4
2	6.2	58.6	10	6.8	72.0
3	5.8	58.7	11	5.7	60.3
4	5.7	50.9	12	4.8	56.1
5	5.4	63.0	13	5.5	59.3
6	6.0	60.0	14	6.9	79.8
7	6.3	67.0	15	5.2	63.7
8	4.9	58.0		Aver. 5.7	

TABLE 6.—HYDROGEN-ION CONCENTRATION OF URINE COMPARED WITH PLASMA BICARBONATE OF INFANTS FED ON PROTEIN MILK

Case No.	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Plasma at 0° and 760 Mm.	Case No.	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Plasma at 0° and 760 Mm.
1	4.2	54.6	9	5.3	62.1
2	4.8	58.1	10	4.2	60.0
3	5.6	63.2	11	4.7	54.3
4	5.8	61.0	12	4.8	55.8
5	6.0	71.0	13	5.9	61.0
6	4.6	60.0	14	6.2	76.1
7	4.3	58.0	15	4.7	59.8
8	5.1	66.0		Aver. 5.08	

Cases of Acidosis.—The results from fourteen cases of acidosis are shown in Table 9. The hydrogen-ion concentration of the urine is uniformly high, but the individual figures are no higher than some observed in infants without acidosis. With the correction of acidosis the hydrogen-ion concentration is lowered, as would be expected.

TABLE 7.—HYDROGEN-ION CONCENTRATION OF URINE COMPARED WITH PLASMA BICARBONATE OF INFANTS FED ON DRIED MILK *

Case No.	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Blood Plasma at 0° and 760 Mm.	Case No.	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Blood Plasma at 0° and 760 Mm.
1	4.1	53.6	9	4.7	54.0
2	4.6	55.0	10	4.7	57.0
3	4.7	56.7	11	5.9	69.4
4	5.0	55.3	12	4.6	58.1
5	5.0	58.6	13	4.8	56.2
6	4.8	59.0	14	5.4	66.4
7	5.3	66.0	15	5.7	62.0
8	5.0	63.0		Aver. 4.95	

Average total (Tables 5, 6 and 7), 5.24

* The mixtures fed represented approximately 1.5 to 2 per cent. of fat, 4 to 5 per cent. of sugar and 3 to 5 per cent. of protein.

TABLE 8.—INFLUENCE OF FOOD ON THE HYDROGEN-ION CONCENTRATION OF THE URINE

Food	Hydrogen-Ion Concentration of Urine	Plasma Bicarbonate; C.c. of CO_2 Bound by 100 C.c. of Blood Plasma at 0° and 760 Mm.
Baby W.—		
Protein milk	4.8	57.6
Protein milk and potato gruel	6.3	63.7
Dried milk	4.3	56.7
Dried milk and potato gruel	6.0	59.3
Baby J.—		
Milk and water mixture	5.4	58.6
Milk and water mixture and potato gruel	6.3	61.4
Dried milk	4.6	58.4

The results shown in Table 9 demonstrate the disadvantage of gaging the administration of sodium bicarbonate by the reaction of the urine. The use of such an indicator as litmus, which turns blue at a hydrogen-ion concentration of about 7, would necessitate raising the plasma bicarbonate much above normal. This has been shown by Palmer and Van Slyke.[10] Owing to this disadvantage, Marriott[11] suggests the use of cresol purple (dibrom-cresol-sulphone-phthalein) which changes color at about 5.3. This is much more satisfactory

10. Palmer, W. W., and Van Slyke, D. D.: J. Biol. Chem. **32**:499, 1917.
11. Personal communication.

for this purpose and obviates increasing the plasma bicarbonate much above normal. Even this indicator, however, is not entirely satisfactory, for the urine may be too acid to change cresol purple despite the presence of a normal alkaline reserve. In Cases 1, 2, 8, 10, 12 and 14 (Table 9) the plasma bicarbonate was practically normal, and the urine was too acid definitely to change cresol purple. The same criticism, however, applies to estimation of the hydrogen-ion concentration of the urine.

TABLE 9.—Comparison of Hydrogen-Ion Concentration of Urine with Plasma Bicarbonate in Cases of Acidosis

Case No.	Hydrogen-Ion Concentration of the Urine	Plasma Bicarbonate; Volume per Cent. of CO_2 Bound by 100 C.c. of Plasma at 0° and 760 Mm.	Case No.	Hydrogen-Ion Concentration of the Urine	Plasma Bicarbonate; Volume per Cent. of CO_2 Bound by 100 C.c. of Plasma at 0° and 760 Mm.
1	4.6 5.2	36.3 56.1*	8	4.1 4.8	37.0 60.0*
2	4.8 5.1	41.3 60.0*	9	5.1 5.8	29.0 62.0*
3	4.3 6.4	30.0 78.7*	10	4.2 5.1	33.8 58.6*
4	5.0 7.0	39.3 94.0*	11	4.7 5.7	39.0 60.0*
5	4.1 6.7	32.8 86.0*	12	4.2 5.2	28.7 58.8*
6	4.8 5.4	29.8 54.3*	13	4.5 6.3	31.6 79.0*
7	5.0 6.5	40.0 87.3*	14	4.7 5.1	39.3 54.8*

* After administration of sodium bicarbonate.

On the other hand, the use of cresol purple is of definite negative value in excluding the presence or persistence of acidosis. If the urine causes the development of a magenta or purple color, acidosis can definitely be excluded.

The disadvantage in using an indicator or to show when sufficient bicarbonate has been given is to a great degree hypothetical. Their use in determining the hydrogen-ion concentration of the urine could lead to no more than a slight increase of the plasma bicarbonate. While on general principles it would seem desirable to bring the plasma bicarbonate to normal and no more, yet it has not been demonstrated that a moderate increase in the plasma bicarbonate is necessarily harmful. In this connection Palmer cites a case observed by Tileston in which too much sodium bicarbonate was given and tetany resulted. In several of our cases the administration of large amounts of sodium bicarbonate was followed by tetany, or edema, or both. Whether

these conditions were a direct result of increasing the plasma bicarbonate above normal is difficult to determine. We have observed a number of cases in which sufficient bicarbonate was given to raise the plasma bicarbonate above normal but without the appearance of edema or tetany.

Despite the fact that there is no convincing evidence that an excess of plasma bicarbonate is necessarily harmful, it would seem more nearly ideal to avoid raising the alkaline reserve much above normal. This can be done best by using the plasma bicarbonate as a therapeutic guide. If the determination of the plasma bicarbonate is not possible, the use of such an indicator as cresol purple is desirable. Even if with its use the alkaline reserve is raised somewhat above normal, this condition is of infinitely less danger than that of acidosis.

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FETAL BRONCHIECTASIS *

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There are two types of congenital bronchiectasis: the atelectatic bronchiectasis first described by Heller and Francke, and the fetal bronchiectasis, the first detailed description of which was made by Meyer and Grawitz. The characteristic feature of the former is that, besides the development of an atelectatic condition in the affected part of the lung, there also occurs dilatation of the bronchi by a hypoplasia of the alveolar structure (Hondo). The dilatations are thus changed into various sized, multilocular cavities, with or without open connection with the larger bronchi; infiltration and pigmentation are then absent. On the other hand, there occurs an often marked growth in the cartilage of the bronchial walls. The mucosa is lined with stratified columnar epithelium, usually nonciliated. This type of bronchiectasis is said to appear in later adult life (over 45 years) and results in atrophy of the affected lung.

Fetal bronchiectasis is by far the more rare type. Since the first accurate work of Meyer and Kessler there have been a number of investigations of this interesting condition. Meyer cites Bartolinus, Fontanus, Fabricius, Ludovicus and Nonnus, who described cases which were apparently fetal bronchiectases. Humbert has gathered together several articles in his "Malformation congenitales du poumon." These investigations are concerned, in the great majority of instances, with the possible etiologic factors leading to the production of the condition, and most of the reports of cases include detailed descriptions of the pathologic histology of the lung. However, little or no attention has been given by these observers to discussion of the symptomatology or of the causes of certain concurrent pathologic findings. Furthermore, the opinions as to the etiology of fetal bronchiectasis and its pathologic changes by no means agree.

It is my purpose here to review the literature on this subject, to present a case of this interesting lung abnormality, and to discuss briefly some of the points suggested by this case.

The lung changes occurring in fetal bronchiectasis may cause intrauterine death, developmental malformations in the otherwise normal lung parts or thoracic contents, death at birth, or in infancy or early

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childhood, where the condition manifests itself after a shorter or longer period of latency. Moreover, there are certain cases which undoubtedly belong to this group, in which puberty or adult life has been reached, which have been described as adult forms of bronchiectasis, but which are probably of fetal origin (Schwalbe).

The condition is one in which there develops in the lung smaller or larger cavities, sometimes involving only part of a lobe, again the whole lobe, occasionally more than one lobe on one or both sides, and which, as Grawitz first ascertained, are of bronchiectatic nature. The affected portions are occasionally only slightly enlarged, but usually show great enlargement, sometimes causing considerable displacement of the heart and other thoracic contents, and at times, as in my case, consuming almost all of the space available in the thorax. Grawitz divided fetal bronchiectases into two types — "die telangiectatische angeborene und die universelle angeborene Bronchiectasien." The first type produces a cystic degeneration of a whole bronchus with all its branches and simulates an ovarian cystoma, while in the second type one finds small cystic ectasies which impress one as dilated lymph channels and are even more similar to a ranula pancreatica (Hondo). Kaufmann differentiates two types which are apparently but different grades of the same process, and which are seldom seen in the same case. In the one type, the affected portion is more or less completely composed of small cavities, those situated subpleurally and meeting with less resistance, becoming the largest, often attaining the size of a pea. The lung presents a spongy, emphysematous appearance, and the cavities, which, separated from each other by thin falciform septa, appear to lie in rows, may be connected with the larger bronchi or completely shut off from them (*Wabenlunge*). In the other and much more rare type, the entire lung segment is changed into a large cyst, on the inner wall of which numerous falciform septa form small pocket-like spaces or are completely flattened out (*Sacklunge*). There may be no connection whatever with the bronchi or there may be several small connections, which would indicate a single cyst resulting from the confluence of many smaller cysts. Whichever may be the case, the cyst is filled with a watery fluid, sometimes slimy, with air, or, as in my case, with both. This classification, although not exactly the same, seems to coincide with that of Grawitz.

Grawitz considered his first four cases (two of these were in collaboration with Meyer) as similar cases of "hydropische Ansammlung bedingte Bronchiektasie," a 5 months fetus, a year old female infant, a new-born child, and a 25 year old male, since in each of these there were similar bronchial dilatations, a single main cyst into which all the side cysts opened. In each case the malformation was localized in a

single lobe which was markedly enlarged. The diagnosis of bronchiectasis was made by the presence of ciliated epithelium and communications with a bronchus. The fifth case of Grawitz, a 4½ months female

Fig. 1.—Gross photograph of thoracic and abdominal viscera, showing large size of lung cyst.

infant, is quite similar to those of Sandoz. Microscopically, the cysts were lined with ciliated epithelium and did not communicate with open

bronchi; the bronchial origin was further indicated by the presence of islands of cartilage.

Grawitz says, "These pictures differ from preparations of the higher grade emphysematous changes found in older people only in the absence of lung pigment." No mention was made of muscle and elastic fiber changes. Sandoz does not consider it improbable that this emphysema was the same as that which appeared in the same parts of his cases where the septa showed bundles of smooth muscle fibers. His cases, which he describes in great detail, were fetal bronchiectases occurring in twin sisters, 18 years of age, and were in many respects similar to those of Meyer and Grawitz.

The cavities are usually lined with ciliated columnar epithelium first described by Grawitz, in some cases flattened out to an endothelial-like thinness; however, they are not, as originally Virchow, and later Klebs, thought, lymphangiectases, since the structure of the walls clearly indicates their bronchiolar origin. The case of Virchow, which he calls a lymphangiectasis, is similar in many respects to Grawitz' last case. The airless lungs of a 9 months cretin had an almost emphysematous appearance, the outer as well as the inner surface showing "protruding cyst-like cavities, singly or in groups, which, when cut open, exhibited smooth-walled, empty cavities." No connection with air cells or bronchi was found, and no microscopic examination was made.

The presence of gland-like canals, supplied with smooth muscle, which have been described by some writers, could not be verified by many others. Sandoz describes narrow, branching, gland-like canals running in all directions, which opened either into the smaller bronchi or into the cyst cavities. The epithelium, where still present, was of the stratified columnar type, ciliated in many places, which, with the concentrically arranged smooth muscle fibers, indicated their bronchiolar origin. The mouths of these tubes frequently showed funnel-shaped widenings and occasionally gave the impression that they had been drawn into the cavities. No alveoli were present in their vicinity. Stoerk refers to them as proof of what he regarded as a tumor-like proliferation, while others describe them as undeveloped bronchi. Stoerk regarded his case as a cystic fetal broncho-adenoma. The right middle lobe of a new-born child contained a tumor the size of a hen's egg, made up of varying sized alveolar-like spaces which reminded him of emphysematous lungs. The cavities into which opened gland-like structures, were lined with simple columnar epithelium and showed muscle fibers in their walls. The connective tissue resembled the embryonic type. The bronchus to this lobe was not found. He described a second case, of the Vienna collection, similar to the first These, like that of Frühwald, in contrast to Sandoz' cases, are localized

malformations of a part of a lung and not a diffuse disease of the whole organ.

The alveoli belonging to the dilated bronchi were often overlooked or not seen, even by careful examinations regarding the elastic structures, although references to well developed alveoli in connection with rudimentary bronchi are not infrequent. In some cases, only the finer, noncartilaginous bronchioles are considered; in others, only those supplied with cartilage are described (Arnheim). Functionally, a communication with a large bronchus is of considerable importance. In many of the cases, complete obliteration was found, the atretic bronchi being indicated only by scattered spots of cartilage. Schwalbe finds in this a great similarity to congenital atresia of the bile passages,

Fig. 2.—Photomicrograph, 4 mm. obj., showing ciliated columnar epithelium of cyst lining.

where, in spite of the closure, dilatation and other defects of the ducts, the remaining part of the gland and bile passages may be well developed, while in some of the cases glandular bronchial growths and bronchial dilatation are the prominent features; in others there appears to be a proliferation of the bronchial intermediates with a tendency toward obliteration.

Almost all of the investigators mention the marked decrease or even complete absence of pigment in the affected parts in contrast to the normal parts of lungs which had functioned for some time.

Couvelaire describes at length the case of a new-born whose right middle lobe was markedly hypertrophic. Distributed irregularly throughout the entire parenchyma were small, air-containing cavities

not more than 1 cm. in diameter, lined with simple cuboidal epithelium. The connective tissue of the septa was of embryonal type. He also found small islands formed by canals lined by high columnar epithelium, which opened into the cyst spaces. None of the medium sized bronchi had the normal appearance. Although these cavities were extremely numerous, they did not prevent easy differentiation of the individual lobes. The alveoli in some places appeared quite normal. Couvelaire says in conclusion, "Il s'agit d'une malformation congénitale bronchopulmonaire aboutissant à des formations kystadénomateuses développées suivant le plan architectural ordinaire du poumon foetal."

Kaufmann mentions two cases and Peiser, one case of fully developed bronchiectases in fetuses. In one of Kaufmann's cases (Case 10) the left lung of a 42 cm. fetus presented the spongy appearance of the honeycombed lung (also described by Box); in the other case (Case 12), the left lung of a 35 cm. fetus was markedly enlarged, 5.5 by 2.5 cm., a typical *Sacklunge*. On section, it had a reticulated appearance, large, branching, smooth-walled cavities occupying the place of the entire parenchyma. Here an open connection with the main bronchus was found.

Hondo's case was that of an infant which was born asphyxiated and died almost immediately. His description is much the same as the others of fetal bronchiectasis. Orth mentions a case of congenital emphysema in a 4 year old child, which he believed to be much like Kleb's case. Löhlein speaks of a cystic papillary lung tumor as the result of a fetal bronchiectasis. Dionisi studied two cases which he considered to be anatomically similar to congenital cystic kidneys, and which he described as congenital polycystic lung degenerations.

As I have mentioned, the opinions as to the cause or causes of the changes occurring in fetal bronchiectasis are widely divergent. The assumption of a merely passive dilatation after a primary bronchial closure is not sufficient explanation on account of the marked enlargement found in many cases, the glandular bronchial proliferation, and further, because in a number of cases there was no bronchial stenosis, Sandoz considers the cavities to be merely the dilated endings of the bronchi. Kaufmann wrote, "To understand this peculiar change one must think of an hypoplasia which permits of the greater development of the larger bronchial branches, but not of the alveoli." "In certain cases," he adds, "the bronchial dilatation occurs through the retention of secretion behind a bronchial stenosis." In this connection, Virchow and Klebs thought of lymphangiectasis.

Stoerk, observing a case of excessive epithelial proliferation, considered it a fetal broncho-adenoma, which Hondo agrees must be

thought of. However, even if it must be admitted that these changed lung parts may furnish the basis for lung tumors, it seems that an explanation of the development of fetal bronchiectasis by the presence of epithelial proliferation alone is not sufficient; the mesenchym and bronchial dilatation must also be considered. The opinions of Kimla and Couvelaire, that the condition results from a disproportion in the mesenchymal and endodermal anlage of the lung, seem very plausible.

Several writers assume, from the histologic pictures of their cases, that the condition is due to an inflammatory process. Hondo believes it to be due, not to a disturbance of secretion, but to an inflammatory

Fig. 3.—Photomicrograph, 32 mm. obj., showing character of cyst wall. Note cartilage and blood vessels.

process of early embryonic life. Sandoz described marked leukocytic and lymphocytic infiltration, cellular proliferation and degeneration, and concludes, "We have two processes here — the malformation of the bronchi and the inflammatory process." He adds that the air pressure of postfetal life must be considered a factor in the production of the bronchial dilatation in the malformed parts. He does not believe it possible for the retention of secretion to cause a bronchiectasis, and, in his cases, found open communications with larger bronchi. He says further, "The inflammatory process present in the malformed parts affects the bronchi and peribronchial connective tissue, and the lung parenchyma equally, and must be considered as well as the process of malformation."

The earlier investigators, among whom existed the tendency to attribute the condition to intra-uterine inflammatory processes, soon brought forward the explanation of congenital syphilis as the causative factor. Sandoz emphasizes the point that his cases were twin sisters, and that the cause of the bronchiectasis occurring in both cases must have been some influence either transmitted to the ovum or forced on the embryos during pregnancy. Although he had no proof for an assumption of syphilis, either from the histories of the cases or from the examination of the other organs, he suggests syphilis as a probable explanation, and finds a similarity in his cases to the lung findings in congenital syphilis.

Stroebe and Spanudis mention the interesting point that syphilitic lungs now and again do not attain alveolar development. Arrest in development certainly occurs in the lungs, as in the kidneys, etc., but what happens later is not known. Bronchiectasis has, however, been described by the French writers in connection with hereditary syphilis. Aufrecht also described a marked dilatation of the smaller bronchi in congenital syphilis. Balzer and Grandhomme described a case of a luetic child, which died soon after birth, and whose upper left lobe had the appearance of a greatly enlarged cystic kidney. The hazelnut sized cysts contained a cloudy liquid, and microscopically appeared to be of bronchial origin. They suggest the similarity of this case with the first case of Grawitz, who, however, made no mention of syphilis. They describe ampulla-like dilatations of the smaller bronchi in the normal lobes, and found, also, a chronic bronchopneumonia with prominent foci in the peribronchial and perivascular connective tissue, and less marked foci in the alveolar septa. They considered that in their case syphilis was merely a coincidence.

Spanudis lays stress on the fact that in luetic lung processes, the proliferation and desquamation of the epithelium go hand in hand with the interstitial process. Birch and Hirschfeld emphasize the peribronchial and perivascular localization of syphilitic interstitial pneumonia.

There are very few descriptions of the lung findings in late hereditary syphilis, and these are quite brief. Fournier found in 212 such cases that the lungs were involved in only five cases. Gummas occurred in four cases; in a fifth case (Lancereaux), in a 41 year old woman, the right lung was partly involved by bronchiectatic cavities the size of a pigeon's egg or smaller, lying in indurated tissue. Unfortunately, no microscopic description was given by Lancereaux. Virchow described an alveolar catarrh in connection with white hepatization.

Aufrecht, referring to other observations (Rollet, Schnitzler, Hiller, Pavlinoff), says that syphilis may be looked on as the basis of all

diffuse pneumonic diseases. Stoerk describes processes quite like peribronchitis and periphlebitis. Flockemann concludes, however, that the indurative fibrous process does not simulate syphilis, and that the changes described by investigators of bronchiectasis may well be affected by other disease causes, but he does not suggest specifically what causes.

Pepere and Dionisi are of the opinion that this condition is due to congenital disease. Pepere also suggests that many cases appear to be the result of a congenital lack of resistance of the whole lung tissue, particularly the stroma.

Regarding the effect on the normal lung parts, it is quite possible that the rapid and increasing enlargement of the bronchiectatic lung part may have an injurious effect on the normal parts, and, as in the case of such spreading processes, produce a circulatory disturbance. Frühwald speaks of a case of intercostal lung hernia due to fetal bronchiectasis.

The tendency of most of the modern writers is to assume that the change is the result of a developmental derangement through which the different parts of the bronchial tree reach an incomplete and disproportionate development, in which the formation of alveoli is absent. The different appearances in the various cases may, according to Schwalbe, be explained by the site and degree of the dilatation. The microscopic proof of nondevelopment or maldevelopment and the simultaneous occurrence of other abnormalities favor this theory of a primary maldevelopment.

A congenital basis for some cases of bronchiectasis is accepted, partly occasioned by the reference to an instance of heredity (Neisser and others). The French writers in particular assume a congenital "debilitas pulmonalis," "maladie kystique" (Peiser, Humbert), a congenital lack of resistance which, on account of the normal requirements of the lungs, points the way to the development of a bronchiectasis, and Humbert suggests an inhibition of the postembryonal growth of the bronchial wall.

My case is that of a new-born child and is in many respects similar to the other cases of fetal bronchiectasis of the *Sacklunge type*. Nowhere, however, have I found an analysis of the cyst fluid such as I have made.

REPORT OF CASE

History.—A new-born child (W.) whose family history was negative for syphilis, malignancy, tuberculosis, etc.

Past History of Mother.—Para I, 26 years of age; had the usual diseases of childhood, but no serious illnesses. Her first labor terminated thirty months previously by a difficult midforceps delivery; she had a nonfebrile puerperium and nursed her child for eight months; the child is in excellent condition at present.

Present History.—Multigravida. Last period occurred Sept. 29, 1917; she felt life eighteen weeks later. Pregnancy was normal throughout, with no vomiting; urine was normal on weekly examination; blood pressure, systolic, ranged from 115 to 120. Since the baby was estimated to be considerably larger than the first child, which weighed 3,210 gm., and the labor which was due July 15 had not started, the patient was given 10 grains of quinin sulphate and 2 ounces of castor oil at 9 a. m. July 16, and the quinin repeated in one hour. Labor started at 10 a. m.

The baby, a female, weighed 3,438 gm., and was 52 cm. in length. It was noticed that the child exhibited a very slight bluish tinge; however, it cried quite normally. No abnormality was detected by casual examination. The child was apparently well formed and well developed. No special examination of heart or lungs was made.

One hour after delivery it was noticed that the child was dyspneic and markedly cyanotic. All efforts to overcome the apparent asphyxia were unsuccessful and included artificial respiration, hot tubbing, oxygen, and intramuscular administration of camphor oil. The respiratory efforts came at increasing intervals and the child died one hour and thirty minutes after birth.

Necropsy.—The body is that of a female, newly-born infant, 52 cm. in length, apparently well developed and well nourished. The skin is elastic and everywhere markedly cyanotic. No edema, eruptions, abrasions, hemorrhages, desiccation, or other abnormal discoloration.

The head is well formed, of normal size and shape, and covered with a moderate amount of brown hair. The sutures and fontanels are of normal size. The pupils are equal and normal in size and shape. The sclerae are of normal appearance. The neck, thorax, abdomen, genitals and extremities present no abnormalities or malformations.

The pericardium presents the normal size, appearance and relations, and contains the normal amount of fluid.

Lungs: No pleural adhesions or fluid. The right lung presents a normal appearance and weighs 7 gm. On section, a small amount of whitish, foamy material can be expressed from the bronchioles. The lower left lobe presents an atelectatic appearance. The upper left lobe presents a large air- and fluid-containing cyst with the unexpanded lung tissue spread out over its surface. The cyst contains 75 c.c. of fluid (described later) and a lesser quantity of air. No connection between the cyst and a bronchus can be determined. The wall of the cyst is covered irregularly, but completely, with strands of white, fibrous tissue of varying thickness and irregularly distributed, incomplete, falciform septa, partially walling off varying sized pockets from the main cavity. No secondary cysts are to be seen. Sections of lung tissue from this lobe sink in water, whereas other sections float.

Heart: The heart, in situ, lies with its base in the right anterior axillary line and its apex in the midsternal line; no pericardial fluid, adhesions, or thickening. The size, color, shape, and consistency are normal and it weighs 13 gm. The ductus arteriosus and foramen ovale are patent and normal.

Measurements:	Mm.
Thickness of wall of left ventricle	2.5
Thickness of wall of right ventricle	3
Circumference of mitral orifice	32
Circumference of tricuspid orifice	38
Circumference of aortic orifice	20
Circumference of pulmonary orifice	21

The peritoneal cavity is free from adhesions, exudation, etc. No distention, contraction, or abnormal development of the intestines is present. The lymph nodes are of normal size and color. The intestines are 4.45 meters long. Mucous membranes present a normal appearance throughout.

The spleen lies in its normal position and presents no abnormalities in color, etc. The capsule is normal; the trabeculae, lymph nodules, pulp and blood vessels are normal. The spleen weighs 10 gm. and measures 5 by 3 by 1.7 cm.

The liver shows no enlargement or other abnormal appearance and cuts with normal resistance. It weighs 100 gm. and gives the following measurements:

	Cm.
Length, right to left	9
Vertical diameter of right lobe	6
Vertical diameter of left lobe	4.7
Average thickness	3.5

The adrenals present no abnormalities and together weigh 4 gm.

The kidneys exhibit the surface markings of the fetal lobulations, but no pathologic appearance as to size, shape, color, or consistency. The capsule strips easily. The cut surface presents a normal appearance; the cortex measures 2 mm. and the entire kidney substance, 12 mm. The kidneys measure 4.3 by 2.7 by 1.9 cm. and weigh 10 gm. each.

The thymus presents no abnormality and weighs 5 gm.

Anatomic Diagnosis.—1. Cyanosis of the skin. 2. Cyst and atelectasis of the upper lobe of the left lung. 3. Incomplete expansion of the lower left lobe. 4. Hypertrophy of the right ventricle.

The sections cut for microscopic examination were fixed in formaldehyd solution, imbedded in paraffin and stained by the usual hematoxylin-eosin technic.

Microscopic Examination.—The sections of kidney, spleen, liver, pancreas, intestine, thymus, and suprarenal exhibit no pathologic appearances other than the usual post mortem changes. Sections of lung and liver, stained according to the method of Levaditi, exhibited no treponemata. In the sections of suprarenal body may be seen a rather distinct zona glomerulosa, said not to appear until the second or third year.

Heart: Sections of the right ventricular wall show an increase in the transverse diameter of the muscle fibers and well stained, square-end nuclei. Otherwise these and other sections are quite normal.

In order to avoid repetition I will describe the microscopic appearance of the various cyst wall sections as a composite picture. In some places the flattened pleural epithelial cells and the underlying thin layer of connective tissue have a normal appearance, in others they are absent, while frequently the pleura may be seen to be somewhat thickened. Beneath the pleura lie various sized areas of unexpanded lung tissue, some very large areas showing no alveoli whatever, or only indications of them. They appear to be areas of undeveloped lung in which there remains considerable mesoblastic tissue, a rudimentary type of connective tissue, considerable lymphocytic infiltration, especially about the blood vessels, a few leukocytes, and occasional plasma cells. The nuclei of the stromal cells are large, round and well stained. The round or spindle shaped cell bodies stain rather poorly. The stroma is relatively rich in blood vessels, mainly small arterioles and capillaries. Most of the alveoli which are present are unexpanded; the epithelium, which has largely desquamated, appears irregularly cuboidal in places, and the nuclei occasionally seem to bulge into the lumina. Here and there throughout the stroma are small placques of irregularly arranged smooth muscle fibers. Blood pigments may be seen in some places; anthracotic pigment is, of course, absent. The bronchi show dilatation and, in some places, epithelial proliferation, and the normal bronchial glands are frequently to be seen. The cyst wall is made up of fibrous tissue in which occur smaller or larger pieces of hyaline cartilage, the connective tissue between them being extensively infiltrated with lympho-

cytes and a few leukocytes. Here, also, varying sized placques of smooth muscle fibers are frequently seen, in some places lying between the cartilage and the epithelium. No secondary cysts were seen.

The epithelium, largely desquamated, is of the ciliated columnar type, sometimes appearing as a single layer and sometimes stratified, where the underlying cells assume a cuboidal or round shape. In a few places the epithelium appears to lie on a well developed basal membrane. Beneath lies a thick layer of connective tissue quite infiltrated with lymphocytes and a few leukocytes.

Lying among the islands of cartilage, are rows of cells with heavily staining nuclei, which seem to be of bronchiolar epithelial origin. Here, also, are various sized areas of glandlike tissue.

Sections from the right lung show slightly dilated alveoli, the interalveolar connective tissue with the contained blood vessels being somewhat thinned, indicating a moderate grade of emphysema.

Sections from the lower left lobe show large areas of unexpanded lung tissue similar to those mentioned before in the upper lobe.

Microscopic Diagnosis.—1. Fetal bronchiectasis, forming a cyst of the upper lobe of the left lung. 2. Atelectasis of both left lobes. 3. Alveolar dilatation of the right lung, slight. 4. Slight myocardial hypertrophy of the right ventricle.

Analysis of the Cyst Fluid.—Amount, 75 c.c.; specific gravity, 1.009; reaction, slightly alkaline (litmus); appearance, slightly cloudy or opalescent fluid, of light-yellowish color, noncoagulated after standing at room temperature for five days.

Microscopic examination showed an occasional polymorphonuclear leukocyte, less than 3 per cubic millimeter, which may be due to error in collecting the fluid, and fat globules which stained well with Sudan III; no crystals were to be seen. Quantitative determinations of the cyst fluid constituents gave the following results calculated in parts per 1,000:

Water	987.77	
Total solids	12.23	
Fibrinogen[1]	trace	
Albumin[2]	2.38	
Fats and lipoids[3]	0.26	
Water extractives	9.61	
Ash from water extractives	8.85	
Ash from water insoluble bodies	0.62	9.47

The ash yielded 3.79 parts chlorin[4] per 1,000 and qualitatively showed a small amount of sodium. Cholesterin, lecithin, uric acid and urea determinations were, unfortunately not made.

Most of the histologic features of this case are quite similar to those found by most of the observers; for example, the somewhat thickened pleura, the areas of unexpanded lung, the cellular infiltration, the irregularly distributed muscle fibers in the stroma, the dilatation of the smaller bronchi, the epithelial proliferation, the placques of smooth muscle fibers lying between the epithelium and cartilage, the cartilage islands, the thick connective tissue layer below the epithelium, and the

1. Determined according to the method of Whipple.
2. Determined by Scherer's method (Webster).
3. Determined by Röse-Gottlieb method (Rupp-Müller).
4. Precipitated as silver chlorid (AgCl); calculated as chlorin.

ciliated columnar epithelium lining the cyst. Addison and How have described the cuboidal epithelium of fetal alveoli such as I have mentioned above. Concerning the bronchiolar epithelial cells, the islands of cartilage and the intermingled placques of smooth muscle fibers, I have considered these in relation to the cyst wall, partly because of the comparatively large size of these areas, whereas one must also consider the possibility of their relation to imperfectly developed bronchioles in the cyst wall, perhaps interfered with in their development by the enlargement of the cyst. That the increasing enlargement of the cyst could produce a mechanical interference in the development of neighboring bronchi is readily conceivable, as I have indicated before. Furthermore, the increased resistance offered to the circulation by the development of the cyst, as is the case in almost every instance of a growing process occurring in the thorax, as well as by the atelectatic lung, may be quite sufficient to cause the myocardial hypertrophy apparent in the preparations of the right ventricle.

If it is proper to interpret the muscle and cartilage as belonging to the cyst, then there can be no doubt as to its bronchial origin. Proof of such origin, however, is certainly to be had in the ciliated columnar epithelium of the lung and in the thick layer of connective tissue beneath it. The fetal alveolar epithelium is not of the ciliated columnar type and it is difficult to conceive of a metaplasia into a more highly differentiated form. Hence, it is quite justifiable to assume that we are dealing in this case with a fetal bronchiectatic cyst. Furthermore, if it is true that the lungs may be said to have completed their development by the sixth week of intra-uterine life (Ballantyne), then the cause or causes of the condition must have been present in the ovum or forced on the embryo during the first six weeks.

As to the etiology of this condition nothing positive can be said. Syphilis, I think, can be eliminated; it is certainly not pneumonia gelatinosa specifica, there are no miliary syphilomas with signs of neighboring interstitial pneumonia, nor is there the connective tissue hyperplasia indicating a clearly marked interstitial fibroid pneumonia—pneumonia interstitialis fibrosa chronica congenita. The areas of undeveloped lung with remaining mesoblastic tissue, which I have mentioned before, may suggest pneumonia alba syphilitica, but the other features of the case, together with the absence of any positive evidence of syphilis in the family, and of treponemas in the liver and lung, clearly point against syphilis.

One feature of this case is of particular interest, namely, the composition of the cyst fluid, which so closely approximates that of amniotic fluid. Liquor amnii is described in various places as a

serous fluid of slightly alkaline reaction, and has a specific gravity varying from 1.006 to 1.013. Its composition at term has been determined as the following.

Investigator	Water Per Cent.	Solids	Albumin	Water Ext.	Fats and Lipoids	Salts	Chlorids
Ballantyne	97 to 99	1 to 3	0.6 to 1	0.03 to 0.7	.....	0.3 to 0.9	0.586 (NaCl)
Labruhe	99.15	.....	0.082	0.06	.....	0.706	
	98.793	1.207	0.2533	0.1689	0.0368	0.1464	0.5596
Winckel	.....	.....	0.24 0.22	.....	.....	(Sod. Phos.)	

The question arises as to the possibility of the cyst fluid being liquor amnii. Addison and How found that during prenatal life the future respiratory passages are filled with a liquid, which, with the first inspirations, is drawn into the lungs. Intra-uterine respiratory movements have been described by several clinical observers (Ferroni and others). Howell expresses the opinion that the mammalian fetus under normal conditions makes no respiratory movements while in utero. Ballantyne accepts the results of the clinicians, but says it is doubtful that they are strong enough to draw liquor amnii into the lungs. Addison and How add that if the movements are really similar to respiratory movements, "they are not to be compared in point of intensity with the postnatal efforts, and do not affect the structure of the lung to any extent." Leclard, on opening the trachea of a still living guinea-pig fetus, found a fluid analagous to amniotic fluid, and that when colored fluid was injected into the amniotic fluid, that in the bronchi was also colored. This was verified by Preyer and added to by Geyl.

The presence of fluid in the alveoli and bronchioles does not seem to me to be entirely dependent on respiratory efforts, in that the normal development of the growing air spaces could well explain it. The fluid must be either liquor amnii or that secreted by the bronchial glands; its composition in this case and the observations noted strongly suggest the former, but this cannot be definitely proved. However, its composition is quite unlike the secretions.

Lastly, I wish to suggest certain possible explanations for the child's air hunger and cyanosis. These can be explained, according to the recent work of R. G. Pearce, as due to increased carbon dioxid tension in the blood, and anoxemia, respectively. In this case the cyanosis appeared immediately after birth and increased in intensity until death. Three factors may contribute to the production of the cyanosis in this case: First, the atelectasis prevented the aeration of the blood passing through that part of the lung; second, the increased resistance to the circulation on the affected side may have been suffi-

cient to cause the flow of considerable unrespired blood through the patent ductus arteriosus into the systemic circulation. Both of these causes could have brought about the presence of unrespired blood in the general circulation, that is, blood with a low oxygen content. Added to these is the third factor, that the great size of the cyst was enough to prevent the advent of a sufficient quantity of air for the proper oxidation of the blood even if it could have been available to the blood, as in cases of congenitally large thymus, congenital stenosis of the upper respiratory passages, or any condition preventing the easy ingress of air. Also, it must be remembered that no open connection could be found between the cyst and the larger bronchi, so that complete bronchial stenosis other than that produced by pressure of the cyst must also be considered. It is, of course, impossible to say which of these factors was responsible for the cyanosis; all of them must be considered and probably each had a part.

It is quite probable that the slight alveolar dilatation observed in the right lung was due to forcible respiratory effort, and that the hypertrophy of the heart muscle was due to the increased resistance offered to the pulmonary circulation by the cyst, atelectasis and excess of mesoblastic tissue.

CONCLUSIONS

1. The cause of fetal bronchiectasis is unknown, although the opinion of a primary maldevelopment seems to be current among most modern investigators.

2. The bronchial origin can be said to be proved.

3. The composition of the cyst fluid found in this case strongly suggests the possibility of its being liquor amnii.

4. It appears that there occurred a slight alveolar dilatation of the right lung, probably due to increased respiratory effort, that the myocardial hypertrophy was due to increased resistance to the pulmonary circulation; that the dyspnea was due to increased carbon dioxid tension of the blood, and that the cyanosis can be explained by any or all of three factors — the prevention of oxidation of the blood by the atelectatic state of the lung, the circulation of unrespired blood due to increased resistance to the pulmonary circulation and the patent ductus arteriosus, and the obstruction to the ingress of air by the pressure of the cyst on the large bronchi or by the developmental bronchial stenosis.

I wish to thank Dr. W. D. Fullerton for the clinical history and material of this case, Dr. T. Sollmann for his careful review of the analytical methods and results, and Dr. H. T. Karsner for his interest and valuable suggestions.

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STUDY OF THE INTESTINAL CONTENTS OF NEWLY BORN INFANTS*

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Reports of the *chemical composition* of meconium have been made by Müller[1] and by Zweifel[2] in the eighties of the last century. Since that time no analyses of the inorganic composition of meconium have been made or reported in the literature. The analyses of Müller and of Zweifel were carried out in conjunction with their studies of metabolism during starvation on the professional fasters, Cetti and Breithaupt. According to Zweifel the dry matter of meconium amounts to 20 per cent., whereas Davy[3] in an earlier analysis reported that the dry matter was 27.3 per cent. of the meconium. The total ash was 5.1 per cent. of the dry matter in Zweifel's experiments, and 6.2 per cent. in Müller's. In horse meconium Müller found the ash to be 9.33 per cent. of the dry matter. The following table is taken from Müller's work. The results are expressed in percentage of the ash:

TABLE 1.—ANALYSES OF MECONIUM

	Müller		Zweifel			
	Horse	Human	I Human	II Human	III Human	IV Human
Fe_2O_3	0.80	0.87	1.36	2.60	0.86	0.80
CaO	18.76	8.00	21.80	5.70	5.09	9.50
MgO	2.65	4.32	3.60	4.00	7.23	7.92
P_2O_5	10.21	10.66	7.80	5.40	3.20	8.58
SO_3	38.42	47.05	22.30	23.00	39.50	31.90
Alkalis	21.93	24.42	.....	30.20	.....	23.02
Cl	8.40	.....	3.78	2.53	8.68	3.90
Insoluble in HCl	0.30	0.67				

It will be seen from these analyses that the water soluble portion of the meconium ash is very much larger than the water soluble portion of the feces ash. The predominant feature is the large percentage of alkalis which in meconium is from 21.92 per cent.

*From the Department of Laboratories, Beth Israel Hospital.

1. Müller: Ztschr. f. Biol., 1884, p. 327.
2. Zweifel: Arch. f. Gynaek., 1875; 1886.
3. Davy: In Gorup-Besanez "Lehrb. d. physiol. Chem.," 1862, p. 501.

to 24.42 per cent. of the ash, whereas in dogs fed on meat, the ash of the feces contained 4.5 per cent. alkalis. The alkalis are in a large measure, as Zweifel has pointed out, in union with sulphuric acid and the observation of certain older authors that there is no sulphur in meconium is an error. The fact that there is such a large excess of water soluble substances in meconium shows that the absorption of the fetal alimentary canal is poor. The large amount of sulphur present (as compared with the feces of starving subjects) can be explained on the basis that the taurin excreted in the bile in the form of taurocholic acid is not liberated and reabsorbed during intrauterine life as it is in extrauterine life. On the contrary, the taurin is excreted in the meconium unchanged. A large portion of the sulphur is derived from shed epithelial cells of the intestinal mucosa (Müller).

TABLE 2.—CONSTITUENTS OF MECONIUM (AUTHOR'S ANALYSES)

	I	II	III	IV	V
Parts per Thousand—					
Water	732.3	801.7	784.5	697.7	718.6
Dry matter	267.7	198.3	215.5	302.3	281.4
Organic matter	245.2	180.1	197.7	280.5	257.9
Ash	22.5	18.2	17.8	21.8	23.5
Ash Percentage of—					
Total meconium	2.25	1.82	1.78	2.18	2.35
Dry matter	8.3	9.1	8.2	7.2	8.3
Analysis of Meconium Ash (per cent.)—					
Fe_2O_3	3.17	1.17	2.24	0.92	1.44
CaO	18.24	.....	17.55	21.18	16.34
MgO	4.21	8.05	6.17	6.18	4.75
P_2O_5	12.62	8.62	.....	.....	11.70
SO_3	23.14	25.63	18.47	28.30	24.32
Cl	5.86	7.12	6.89	5.34	
K and Na	24.19	.....	33.72		

On comparison of the analyses of meconium by Müller and by Zweifel with their analyses of the hunger feces of the professional fasters, Cetti and Breithaupt, it will be seen that the meconium has lower proportions of calcium, iron and phosphorus, which has been explained by the greater need for these elements in the growing organism as compared with the adult (Cammidge[4]).

We have analyzed the meconium of five infants, voided during the first twenty-four hours of extrauterine life, with the results shown in Table 2.

4. Cammidge: Feces of Children and Adults, 1914.

On comparing our figures (Table 2) with those obtained by Zweifel and Müller on hunger feces (Table 3) we see that there is no great variation in the calcium and iron percentages. This is a distinct difference from the figures obtained by the German authors, and we cannot subscribe to the explanation that the need for lime in the fetus causes a lowering of the calcium content of the meconium. It seems that the need of lime by the growing organism can be compensated by an increased maternal supply. The phosphorus is, however, much lower in meconium, whereas the sulphur proportion is much higher.

Several of the *organic constituents* were also examined. The *total nitrogen* of meconium varies. In a number of specimens analyzed we found from 0.62 per cent. to 1.07 per cent. Traces of *ammonia* were found in all specimens of meconium.

TABLE 3.—ANALYSES OF HUNGER FECES (MÜLLER)

	Cetti, per Cent.	Breithaupt, per Cent.
Insoluble in HCl	1.213	1.780
Fe_2O_3	1.530	3.03
CaO	14.516	12.53
MgO	1.200	4.12
P_2O_5	43.132	55.75
SO_3	6.341	3.71
K and Na	19.620	12.649
HCl	1.320	1.96

Weintraud,[6] in 1895, made the observation that meconium yields 0.1 to 0.3 gm. of pure *uric acid* for every 100 gm. of dry weight. In adults, uric acid is nearly always absent, according to Weintraud, when calomel has been administered. In infants, however, he always found uric acid and the purin bases. He therefore concluded that when putrefaction and processes of reduction, which generally go together, predominate in the alimentary canal, the formation of uric acid is not possible; but when, as in the case of meconium, processes of oxidation are going on, not only is the conversion of bilirubin to biliverdin possible, but there is also a development of uric acid from the nuclein bases. Since meconium is sterile and consists mainly of the products of excretion from the body, these results of Weintraud would tend to support the view that the nucleins are partly of intestinal origin.

6. Weintraud: Die Heilkunde, 1898, p. 67.

Schittenhelm,[7] who also found uric acid in meconium, concluded that it was derived from the swallowed amniotic fluid, and not from the intestinal changes.

So far as the uric acid is concerned, we have been unable to demonstrate its presence in twelve specimens of meconium, and we, therefore, cannot corroborate Weintraud's and Schittenhelm's results or their conclusions.

The *ferments* of the meconium were also studied. From the purely physiologic point of view, it is interesting to examine the enzymic contents of the intestine during intrauterine life. The entire subject of enzyme incidence is encrusted with teleologic conceptions which only time will root out. In intrauterine life, intestinal enzymes can have no function, since there is no food in the intestinal canal. The functions of the pancreas are quiescent, except, perhaps, the function of internal secretion.

Wegscheider[8] demonstrated the presence of *amylase* in infant feces. It was shown by Pottevin[9] that it is constantly present in meconium. This was confirmed by Hess. No quantitative studies of this enzyme in meconium was, however, ever made, and we determined to analyze fifteen specimens of meconium from fifteen infants quantitatively for pancreatic amylase by the method of Wohlgemuth[10] as modified by Hawk.[11] We obtained the results given in Table 4.

It will be seen that while the starch splitting enzyme is, it seems, present in meconium, its quantity is very much reduced. We did not filter the meconium through a Berkefeld filter, and we cannot state whether the traces of amylase found were not in reality results of bacterial digestion, the bacteria having contaminated the meconium during the process of collection. In spite of the fact that it can have no function in the early months of extrauterine life, the amylase is present in increasing quantities in infants' feces.

Orban[12] found *lactase* in the intestinal mucosa, and it was later demonstrated in the feces of infants. Lactase is formed, according to some observers, by the epithelial cells of the alimentary mucous membrane, but Martinelli[13] observed it also in the pancreatic tissue. We have been unable to find lactase in any of fifteen specimens of meconium.

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7. Schittenhelm: Zentralbl. f. d. ges. Physiol. u. Pathol. d. Stoffwechs., 1909.
8. Wegscheider: Dissertation, 1875.
9. Pottevin: Compt. rend. Soc. d. biol., 1900, p. 589.
10. Wohlgemuth: Biochem. Ztschr. **9**:1, 1904.
11. Hawk: Practical Physiological Chemistry, 1917.
12. Orban: Prag. med. Wchnschr., 1899, p. 427.
13. Martinelli: Zentralbl. f. d. ges. Physiol. u. Pathol. d. Stoffwechs., 1907, p. 481.

Trypsin is normally present in the feces of children and adults. It has been reported by some observers, Hess and others, that pancreatic protease is present in meconium. We have been unable to find trypsin in the freshly voided specimens of meconium during the first day of extrauterine life. Eight individual specimens were examined with constant negative results. We present these findings with reserve, for we are aware that we contradict the observations of a number of children specialists. We used the method of Gross[14] for the trypsin analysis. We have also applied Spencer's technic in an endeavor to apply a very delicate test. As Schmidt and Strassburger[15] suggest that the trypsin which is reported present may be, in a large percentage of cases, due to *erepsin*, we examined several specimens of meconium for erepsin, but we cannot report any success. The results were invariably negative.

TABLE 4.—AMYLASE IN MECONIUM

Specimen	Dm $^{38°}_{24h}$ *
1	12.1
2	11.7
3	10.9
4	0.0
5	11.1
6	0.0
7	12.4
8	10.7
9	10.8
10	10.4
11	0.0
12	?
13	?
14	12.2
15	10.3

* Dm $^{38°}_{24h}$ signifies the diastatic digestion of 1 c.c. of pure meconium at 38 C. incubated for twenty-four hours. The figures in the table represent the number of cubic centimeters of a 1 per cent. starch solution digested by 1 c.c. of meconium for twenty-four hours at 38 C.

Lipase was found by Hecht[16] in sucklings' feces in the very earliest days of life. Schönberner[17] found lipase in meconium (1909). This was Schönberner's research for his inaugural dissertation at Munich.

14. Gross: Deutsch. med. Wchnschr., 1909.
15. Schmidt and Strassburger: Die Feaces des Menschen, 1910.
16. Hecht: Wien. klin. Wchnschr., 1908.
17. Schönberner: Dissertation, Munich, 1909.

His experiments and conclusions are to be strictly scrutinized, for, no doubt, he has permitted a number of errors to enter his experiments. We have found no lipase in fresh meconium voided during the first twenty-four hours of life.[18]

CONCLUSIONS

1. The inorganic composition of the meconium is reported, five specimens having been analyzed. The iron and calcium contents are similar to those obtained in hunger feces. The phosphorus of meconium is less. The sulphur is much increased.

2. Traces of ammonia were found in meconium.

3. No uric acid was found in twelve specimens of meconium examined. This fails to corroborate Weintraud's analyses.

4. Amylase is found in the meconium in extremely faint traces.

5. Neither trypsin nor erepsin were found in eight specimens of fresh meconium.

6. No lactase was found in meconium.

7. No lipase was found in fresh meconium.

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18. Consult also, Ury: Arch. f. Verdauungskr., 1908, p. 411; Biochem. Ztschr. **23**:153, 1909.

SLEEP IN CHILDREN AND ITS DISTURBANCES

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REMARKS ON PHYSIOLOGY OF SLEEP

Czerny[1] in his investigations of the sleep of children examined its depth and intensity under physiologic conditions; he used, as stimulus, the opening induction current, with increasing intensity, until awakening occurred. He demonstrated that the depth of sleep in healthy children depends on the period of sleep.

In very young nurslings after satiation sleep reaches its greatest intensity within the first hour, whereupon a very slow decrease ensues; after an average duration of sleep of three hours awakening takes place for the purpose of feeding. In older infants this sleep lasts somewhat longer. In two infants, 9 months old, the curve of the intensity of sleep (Fig. 1) during the whole night, demonstrates in Czerny's experiments two parts, separated from each other by a short waking interval, the maximum of depth of the second period being much less than that of the first period. The waking interval is due to the increasing desire for food, and, indeed, the former is absent, when, with the growing age of the children, the hunger stimulus becomes less and no more suffices to awaken them.

In six children between 2 and 6 years of age, who used to stay awake the whole day and slept throughout the night, the depth of sleep attained its maximum within the first hour, decreased during the second hour rapidly (Fig. 2), later more slowly, reaching its minimum in the fifth or sixth hour, and increased a second time in the morning. This second ascent of the curve, occurring in the ninth or tenth hour, however, did not reach the maximum of the first hour. This character of the curve suggests two periods of sleep by a continuous combination of the two foregoing night curves illustrated in Figure 1.

Similar experiments, it seems, have so far not been undertaken in older children, but it is assumed that their night curves may more and more approach those found in adult life, by Kohlschütter, Moenningshoff and Piesbergen, and recently by Michelson. Moenningshoff and Piesbergen determined the depth and intensity of sleep by finding the threshold value of an auditory stimulus necessary to wake the person at different intervals after he fell asleep. They found the attached

1. Czerny: Jahrb. f. Kinderh. **33**:1.

curve (Fig. 3), which is self-explanatory, the abscissae representing the duration of sleep, the ordinates the intensity of the stimulus necessary to awake.

Michelson's very exact investigations revealed two types of curves, representative of the depth of sleep in the adult. In the first type (Fig. 4) the sleep becomes rather rapidly profound, reaches its maximum in about the first hour and becomes in a short time shallow, maintaining after a few hours only a moderate degree of depth. With the representatives of the second type (Fig. 5) the sleep deepens slowly, obtains its maximum depth, that is less than in the previous type, not until after one to three hours; it then becomes shallow more slowly than in the first type, and remains even in the fifth and sixth hours rather deep.

These two sleep qualities seem to have a relationship to certain practical facts of life. The first curve is characteristic of those persons who retire early in the evening, fall asleep rapidly and profoundly and awake early in the morning, when they feel completely refreshed and efficient. The second curve (Fig. 5), the "morning type," concerns individuals who retire late, remain until late in the evening efficient, in possession of full, at least sufficient, freshness, but who in the morning require abundant sleep, rise reluctantly and obtain comparatively late their full capacity.

Psychologic experiments testing the mental capacity after normal and shortened sleeping hours, as undertaken by Roemer,[2] reveal interesting data in relation to this subject. They indicate that after awakening, the maximum efficiency is generally obtained only gradually, particularly so by the "morning sleepers." In comparison with their efficiency after a normal duration of sleep, they do not show any decrease of it if they retire later in the evening, since the thus shortened sleep deepens correspondingly in compensation; but their efficiency is very markedly impaired and a state of fatigue results if they are aroused in the morning earlier than they are wont to awake. Evidently, shortening of the morning sleep means to them a considerable loss, since their demand for sleep is then still a great one, as expressed in the depth of the curve toward morning. Individuals of the first type, the "evening sleepers," whose maximum profundity of sleep is obtained rapidly, possess a certain superiority. Shortening of their sleep at evening influences likewise only a little their efficiency the next morning, since the thus curtailed sleep will mostly deepen compensatorily. Still less is their efficiency diminished by shortening the morning sleep, as their requirement of sleep is in the main already satisfied after from three to four hours.

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2. Roemer: Congr. internat. de psychol., München., 1896, p. 354.

These experiments have great importance in the hygiene of school children, inefficiency and fatigue being especially to be noticed after shortening of the morning sleep in children who obtain the maximum of their sleep (Roemer) in the morning. Aschaffenburg[3] observed in some children even as young as in the second and third year of life an obvious tendency to go to rest late in the evening, evidencing then only little tiredness; they would awake late in the morning reluctantlty and with difficulty, sleeping then deeply in spite of the beginning day noises, while other children would rise very early and be lively. In a number of instances I have met with this type. This behavior is not necessarily the effect of education and environment, since both types occur in one and the same family. That in children the demand for sleep in the morning is a greater one than in the adult is indicated by

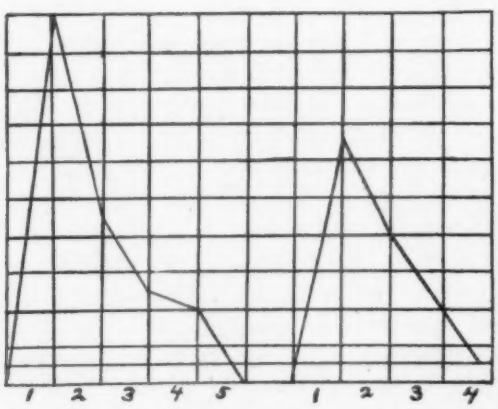

Fig. 1.—Curve of depth of sleep in a baby 9 months old (Czerny).

Czerny's curves. The majority of nervous children, but not infrequently also not nervous children, of school age represent in regard to their sleep requirement the "morning type." Their much reduced efficiency in the morning hours was repeatedly demonstrated by psychologic investigations, measuring the degree of fatigue, and it is the experience of many teachers that particularly nervous pupils are among those who achieve the least in the first hours of the forenoon instruction.

The dotted line in Figure 5 represents the depth of sleep during the darker nights of winter. It would indicate the great importance of darkness of the bedroom and is in keeping with the experience that people who sleep lightly will sleep more deeply and better if the room is completely darkened, whereas many of us will slumber only super-

3. Aschaffenburg: Verhandl. d. Gesellsch. f. Kinderh., 1908, p. 260.

ficially or wake early in the summer, the dawning light acting as a powerful stimulus. We do not know what changes take place in the types as a result of pathologic conditions or change of environment, since experiments have not yet been made; neither can it be stated what other types and transitional forms there exist. Sleep in its physiologic and pathologic phenomena offers abundant interesting problems for experimental investigation and clinical observation in the directions indicated.

CLASSIFICATION OF DISTURBANCES OF SLEEP

Sleep disturbances may be classified from various points of view considering the variety of causes, the pathogenesis, the symptomatology, their relation to other disturbances, etc., and in the presence of the various combinations no classification can be enirely adequate, but bears more or less an arbitrary character. Sleep disturbances may be elementary, concerning the depth and duration, or they may manifest more complicated features and accompanying phenomena; they may be temporary or chronic; due to exogenic factors; or symptomatic, secondary to other diseases; or they may be idiopathic, that is, to a certain extent independent of any exogenic or organic detectable disturbances.

Sleep disturbances accompanying organic diseases. — It would require the presentation of the entire pathology of childhood should one attempt to enumerate all the possible common and uncommon diseases that may directly provoke disturbance of sleep. The latter may often be seemingly the only solitary symptom, whose underlying cause may not be suspected by the inexperienced. Painful conditions must be mentioned first. These dolorous forms of sleep disturbance, or restless sleep, where pain of any origin hinders normal sleep, may be brought about by numerous entirely heterogeneous affections. A most common cause are colic pains, distress and discomfort in gastro-intestinal disorders; even slight nutritional disturbances cause babies to sleep poorly; likewise hunger as a result of a sudden diminution of the wonted amount of food, whilst in chronic underfeeding babies rather often will become accustomed to the small quantities; itching and irritating or painful skin lesions, as eczema, urticaria, strophulus, intertrigo and furuncles, the latter especially if exposed to pressure during sleep. Where sleep-disturbed nights precede the outbreak of urticaria, as I have observed, it is probably due to the at first latent digestive disturbance that underlies both conditions. It is important to keep in mind that otitis media in the child—especially to be considered during epidemics of grip — may evidence itself by no other symptom than moderate fever and sleeplessness, resulting from pain which is not localized by the infant, and thus easily overlooked. That

fever itself with its increased temperature and the accompanying processes may cause sleeplessness as a symptom of the involvement of the nervous system is evident from the sleep-producing effect of antipyresis, be it through drugs or hydrotherapy.

Respiratory obstructions and difficulties, as those due to stenosis of the upper air passages in acute or chronic rhinitis, in adenoids, pseudocroup, dyspnea due to bronchial asthma or cardiac lesions will naturally render the sleep very restless and interrupted; they may cause awakening, starting with gasping for air and feeling of suffocation, or more complicated disturbances, as pavor nocturnus. In one of my observations a severe nocturnal attack of suffocation that frightened the patient and family was traced to penetration into the

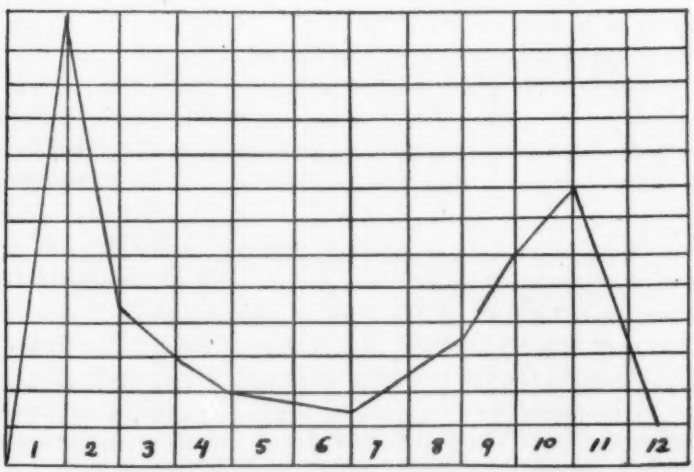

Fig. 2.—Curve of intensity of sleep in a child 3 years and 8 months old (Czerny).

larynx, with resulting severe laryngospasm, of regurgitated hyperacid stomach contents during profound sleep after a heavy supper.

Among the chronic ailments, anemia and rhachitis, especially with craniotabes, will cause restless sleep as a nervous symptom, yielding to a certain extent to phosphorus and cod liver oil. The motor irritation phenomena of chorea minor, tetanus, tetany and athetosis may directly interfere with healthy sleep, as also pollakiuria and polyuria; if the latter symptom be due to partaking of great quantities of liquid before or at bedtime, the abolishment of this habit will within a short time remedy the disturbance.

Extraneous causes, educational factors.—Among the extraneous causes of troubled sleep, namely, those existing in the surroundings, brief mention may be made of a few that are often overlooked by the

attendants and therefore must be pointed out by the physician; deficient ventilation, lack of comfort, lack of quiet and darkness, faulty temperature of the room, with overheating or cooling of the body, exposure of feet in a cold room, lying wet. Too low temperature, insufficient covering will, especially in the morning hours, disturb sleep, as they act as awakening stimuli. The depth of sleep in infants depends on retention of warmth. According to Czerny's observations, infants do not sleep well if they do not come into a state of perspiration and warmth, and his investigations demonstrated that the maximum (perspiration) and minimum of moisture and warmth of skin coincide with the maximum and minimum depth of sleep, respectively. The importance of ventilation, so evident in its beneficial effect on sleep in children who are allowed to sleep on the porch, is not realized by the immigrant from Europe, though among them the ventilation would seem the more imperative, as not infrequently several persons occupy the same bedroom. Discomfort of the resting place comprises also the sleeping in the same bed of several persons, though habit has a mitigating influence.

Unfavorable crowded home conditions of the poor cause the younger children to be habitually deprived night after night of their full quota of sleep by the late retirement of the older persons of the family. Physicians, educators and school workers have repeatedly pointed out that the health and efficiency, especially of children of school age, are injured through such exogenic factors. Occasionally overburdening in school work, too much mental exertion, perverted distribution of the day hours, premature and untimely participation in social affairs and pleasures of the adult, abuse of alcohol, tea, coffee and tobacco, and even sexual stimuli, which later shall be discussed, home work and home industry until late hours, will, by habitually curtailing the minimum sleep requirement, exert a very detrimental effect on the young. Such children soon suffer in their general state of health; the appetite decreases, they often have headache, the mucous membranes lose their healthy hue; skin, muscles and panniculus adiposus become flabby and the youthful, frolicking nature with its love for work is replaced by inattention, fatigue and reduced efficiency in school work; finally, they become nervous and suffer from insomnia, establishing thus a vicious circle.

Idiopathic sleep disturbances.—Idiopathic sleep disturbances are likewise either temporary or chronic, the latter through their great importance being here the subject of closer discussion. Their clinical manifestations are of manifold character; they may be limited to the period of falling asleep, or may continue into the sleep proper, or may concern the latter only.

Stereotypias.—As is well known, children often have the habit of falling asleep in a certain fashion; as, for instance, with their playthings, a favorite toy animal or a doll at their side, or with the corner of the bed clothes or one or more fingers in the mouth; some will, as I have seen, suck the finger only when falling asleep, though not at other times, this being apparently an agreeable sleep promoting stimulus. A nervous girl, 5 years old, for two years had the habit of pulling and twisting the hair over her right temple regularly before sleeping, to such an extent that the hairs there were broken off and shortened in a disfiguring manner. Other children will bite their nails, pull the bed cover over the face, will insist on a certain posture, lying on the stomach, or on the bent knees, or display some other preferred position and habit. The mothers know well these little habits, perhaps being responsible for the development of such stereotypias, and are aware of the fact that the child will refuse to sleep if hindered in this peculiarity. Indeed, if this habitual act is made impossible, as by a

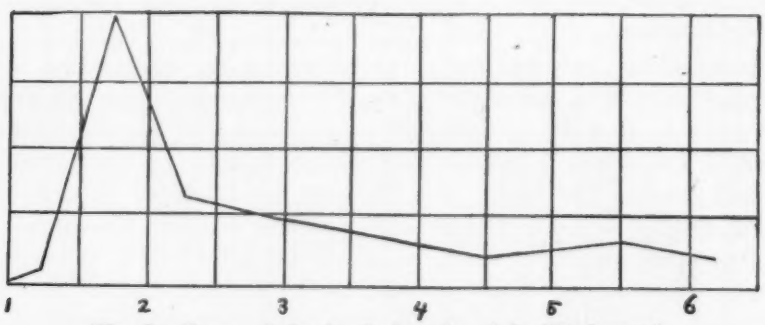

Fig. 3.—Curve of depth of sleep in adult (Piesbergen).

newly appointed nurse, falling asleep habitually associated with the stereotypia may be interfered with for awhile until the cause has been found and relieved, or the child has been calmed in some way or weaned from the habit; in short, has forgotten it. The efforts at quieting the child, as for instance, by rocking or by the mother sitting at the bedside, may through indulgence of the attendant supplant the original habit by a new one. A number of these peculiarities are within the normal; in others the readiness of their development, their singularity, degree and persistency may point to a neuropathic basis.

Motor irritation phenomena.—Some motor irritation phenomena may accompany sleep without awakening the child: jerking of the whole body, twitchings of leg or arm, as by an electric shock, various slow movements with the extremities, rolling and tossing, grinding of teeth, etc. Though they may be observed among otherwise healthy children, and particularly under the influence of some febrile disease, these

phenomena are more frequent among neuropathic individuals. While these motor irritation symptoms have more or less a spasmodic character or are mostly limited to a few muscles, or though coordinate, rather erratic and irregular, other motor manifestations during sleep or at its beginning are more rhythmic, as the jactatio capitis nocturna described by Swoboda and Zappert.[4] Such rhythmic movements were perhaps at first reproduced consciously in the waking state, as they are frequently to be observed, but under certain exceptional conditions become automatic as subconscious and unconscious habits during sleep. In one of my observations concerning a boy, 14 years old, who was affected for many years with nocturnal headrolling, from which also his father and older brother had suffered, the shaking of the head during sleep was so violent and the left lower jaw so forcibly thrown against the left shoulder that its skin showed a red bruised spot as a mark of the repeated impact. He said that by rolling the head he puts himself to sleep.

Dream acts.—While all the motor disturbances so far mentioned are comparatively simple phenomena, there are more complicated psychomotor processes during sleep which evidence the participation of cerebral centers of higher order, namely, irritative conditions connected with the mental processes of sleep—the dreams. Such dreams are not necessarily always the primary factor, but may be due to some other condition that causes irritation of the nervous system. Children, especially those endowed with an excitable imagination, after playing intensely before retiring, may show such evidence of vivid dreams in which their games play an important part. Some children will laugh even loudly, utter certain sounds or speak short broken off sentences; others will sob. A nervous, spoiled child, 22 months old, when crossed by her attendants at sleeping time would sob incessantly, not only during the period of falling asleep but also during the sleep itself, even for two hours. This sobbing, as a reverberation of an affect—whether occurring automatically or under the influence of a dream—also happened throughout the afternoon sleep of the girl.

Some babies suck their tongues during sleep, protruding it between the lips, or push the lips forward as in sucking; these movements being during the waking state among the commonest, may during sleep be merely automatic, since they can be seen even in the new-born and in the state of unconsciousness; but perhaps in older nurslings they may, as Zappert[5] asserts, be transitional forms of dream acts. Dreams in childhood are very frequently the fulfilment of wishes and desires

4. Zappert: Jahrb. f. Kinderh. **62**:70, 1905.
5. Zappert: Wien. klin. Rundsch., 1905, p. 720.

that certainly dominate the psychic life of early age in a much higher degree than in the normal adult.

In these conditions the motor impulses of dream images are transmitted in an activating degree to the cortical psychmotor regions, which in the normal sleep are dormant and inactive. In sleep talking or somniloquy the motor reactions manifest themselves in a variety of peculiarities, anomalies and characters that were the subject of a study by Kreplin, and are in children mostly confined to a low muttering and hardly intelligible talking relating to the experiences of the

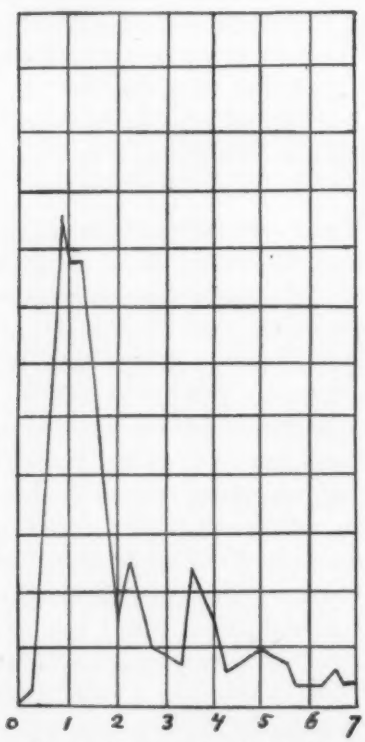

Fig. 4.—Curve after Michelson.

last day. Sometimes the person will also sit up in bed during somniloquy.

Somnambulism. — With sufficient stimulation and irritation of larger cortical and subcortical areas the sleeper may rise from bed, perform complicated acts that have the imprint of a certain deliberation, so different from the motor manifestations that occur without mental processes. They are definite acts, whose motives are dreams. Such dream acts, as exemplified in somnambulism or noctambulism, though rare in the adult and then in connection with hysteria, are fre-

quent in children. Some authors consider somnambulism in children a neurosis by itself or bring it in some relationship to hysteria or epilepsy, or maintain that it may develop from the basis of a general psychoneuropathic degeneration, without corresponding to these entities; it occasionally occurs also in healthy, though perhaps sensitive, but not actually neuropathic persons. Somnambulism is a pathologic exaggeration of the processes of dreams, "a dream mimically performed and spoken." These dreams, as a rule, have no terrifying character, as is the case with night terrors. The somnambulant child rises and leaves the bed without interruption of his sleep, walks about quietly without any affect and performs complicated acts; he may perambulate through the room, carry objects from place to place, busy himself about his school books, make a light, climb upon furniture or leave the room and move about the house. That children in the somnambulistic state should climb out of windows or undertake really dangerous or marvellous performances is generally declared to be rare. If addressed in a low voice, the child may sometimes answer, but otherwise will be undisturbed in his actions; but intense stimuli, as shaking him up, calling him by his name loudly, pricking, pinching or sprinkling him with cold water, etc., will awaken him. If undisturbed he will return eventually to his bed, continuing his sleep. After awakening in the morning there is complete or almost complete amnesia as to the basic dream and acts.

The somnambule by no means performs his actions purely automatically and mechanically, for they are far too complicated for that and presupose deliberation. The patient acts in his twilight state like a person in the dazed state of intoxication. Though he is sleeping and the associations of the normal sensory of the waking state are not at his disposal, certain domains of his consciousness, limited spheres of his brain, are awake and active; under the dominant dream idea he executes movements that are purposive; he acts his dreams. To a certain extent he is unconscious of external impressions; he may have the eyes open and receive pictures on the retina, which, however, do not penetrate to the sphere of clear selfconsciousness, yet by reflex mechanism may guide him and be the starting point of deliberate and definite movements.

That reality-ideas, thoughts and impressions in connection with experiences and events during day life, especially if accompanied by emotions, desires and intentions, should be carried into acts of the dream consciousness in a half reflective way, or that organic sensations (full bladder) may become a provocative element in somnambulistic actions, is not to be wondered at if we consider their relation to ordinary dreams. The following case may be cited:

H. B., a 10 year old boy, who, as also his mother, had suffered from enuresis nocturna, would regularly in the night rise and go to the bath room to void urine, without, however, awakening. Lately he walked, as occasionally had occurred before, into another room, pulled out the drawers of his desk and rummaged in his school requisites. His mother found him there, brought him to the toilet room, where he urinated, and led him back into his bed, without his awakening. On another occasion at midnight he rose from bed, walked to the second floor and there passed urine from the porch. After that he suspended himself by both hands from the edge of the porch and was about to let himself down a 15-foot pole, when a neighbor came up in time to grasp him, still asleep. The boy on previous days had expressed a desire to slide down this pole but was dissuaded. It is noteworthy that loud

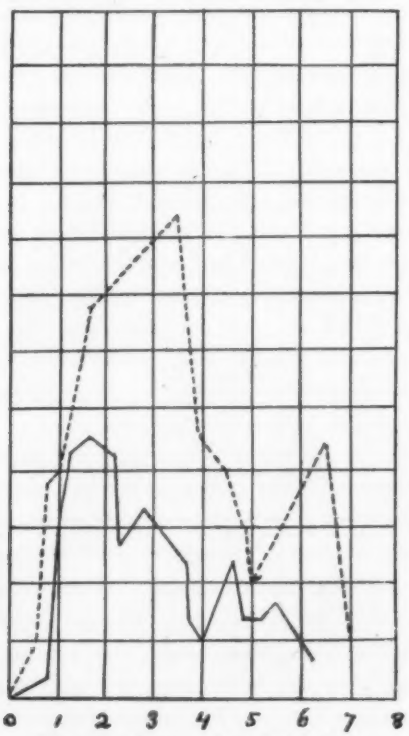

Fig. 5.—Curve after Michelson.

sleep talking is a very regular occurrence with him and that he usually sleeps so profoundly that carrying him about does not awaken him, and arousing him also in the morning is rather difficult.

Children's dreams are more often than in the adult, as mentioned before, simply fulfilments of wishes; thus also in this boy his desire became the motive of a dream act. The following case is a typical representative of the frequent occurrence of a day occupation continuing in dream life and inciting corresponding motor reactions.

A boy, 8 years old, a bed wetter, for a few weeks would frequently during the night whilst sleeping make movements with his arms, as if in ball play, in which he indulged intensely during the day time, drilling for the

closing school exercises; he would also utter words referring to this game. In such attacks, for which there existed complete amnesia, he sometimes would leave his bed and have to be brought back.

Quite unusual on account of the early age and the regularity of the somnambulistic acts is the case of a 3 year-old boy; during the previous year he would rise every night without exception whilst sleeping, crawl out of his bed, move about in the half-dark room, mutter unintelligibly or talk sometimes of the dog, the children, his aunt or such things as occupied him in the day time; he also would climb on the bed railing, crawl underneath his bed, grope about and seek something. These attacks would occur one to four times a night. There was no recollection the next morning. During a recent attack of pertussis the attacks ceased and have not returned.

As a rule if on the part of the attendants no attention is paid to the affection, it soon will disappear, but if in the presence of the child much concern is shown and the disturbance often discussed, it is likely to become aggravated.

That children during sleep irritate their genitals artificially is asserted by some authors. Moll[6] could, through direct observation, establish the fact that occasionally among even young children, boys as well as girls, such nocturnal acts were practiced, not in the waking state but unconsciously during actual sleep with manual or other irritations. He does not, however, state explicitly whether there was a real masturbation with signs of orgasmus, or merely an affectless playing with the parts during sleep.

Pavor nocturnus.—Among the disturbances of oneirogenic origin, that is, in connection with dreams, without awakening, pavor nocturnus, or night terror, has to be briefly discussed. Not infrequently it alternates or is associated in the same individual with somnambulism, sleeptalking, enuresis, originating from a common neuropathic basis. The dreams, terrible in character, may be provoked by physical discomfort, fever, overloading of the stomach or by carbon dioxid intoxication, resulting from respiratory difficulties, as those due to adenoids, acute or chronic rhinitis, enlarged tonsils, or to retraction of the tongue. Boerner, indeed, could produce certain dreams—incubus—experimentally through carbon dioxid intoxication by covering completely the mouth and nose of the sleeper. We must not, however, overlook the many psychogenic causes, for not infrequently it is nothing else but an actual, disagreeable experience of the previous day, that reappears in the dream and assumes a terrifying character. From patients in whom amnesia is not complete, but only partial, or from the incoherent words uttered during the paroxysm, we may learn that these anxious and agitated states are often due to the return of identical, or at least similar, dream pictures in the same child, of so-called stereotyped dreams. Violent shock, fright and somatic trauma, including surgical operations without anesthesia, may become the psychic stimuli for

6. Moll, A.: Das Sexualleben des Kindes, p. 87.

this disturbance that assumes the nature of a traumatic neurosis. A very instructive case was that of Professor Gomperz (quoted from Hamburger[7]), where a boy immediately after adenectomy without narcosis suffered from pavor every night for some time, manifesting elements of fear in relation to the operation. Henoch in his textbook on diseases of children reports the case of a 4-year-old boy who, after having been frightened by a bee manifested a subsequent night pavor which occurred later repeatedly until he was afraid to enter the bedroom. That an imminent operation may disturb the sleep of older children and create disagreeable dreams is often experienced. These and similar observations dispose of the theory that every pavor nocturnus is due to carbon dioxid intoxication. The more vivid the child's phantasy, the more frightened by others or excited by horrible tales, the more readily in predisposed children will night terror occur, which fact carries a warning to the attendants.

While some authors emphasize the relation of night terror to a neuropathic and psychopathic constitution, or place it side by side with anxiety neuroses, others point to the possibility that occasionally paroxysms may occur also among vivid, not nervous children, especially after hearing terrifying stories or attending exciting moving picture performances, when still under their influence at the time of retiring. We all know adult persons of an entirely healthy nervous system who in their childhood suffered from pavor nocturnus, or even later at least from nightmare and other states of anxiety of minor degree. Of course the more marked the constitutional factor, the psychopathic predisposition, the more insignificant may be the provocation necessary to induce an attack.

Night fears may manifest themselves in various degrees and forms. Horrible dreams, for instance, may cause a mere groaning and sighing, feeble crying or screaming without awakening at all, or, in other cases, cause a wild startling and screaming with the sensorium to a certain degree clouded, or cause full awakening with a feeling of oppression and palpitation of the heart, the sufferer being fully conscious of the cause. The recollection might be entirely absent or very indistinct, as is mostly the case also with our ordinary dreams.

Dream pictures which are psychic phenomena in the sensory cortical region will in children not as readily be corrected as in the adult; the children have not yet sufficiently acquired the faculty of distinguishing vivid dream impressions or dream hallucinations and phantasms, especially if accompanied by affects, from reality. In nightmare which occurs rather in older children than in young ones, the child awakes, and, though remaining somewhat under the influence of the dream

7. Hamburger: Monatschr. f. Kinderh. **13**:23, 1914.

image in the grasp of the reverberating fear emotion, he does not continue to hallucinate but recognizes environment and situation, corrects thus the dream idea rapidly and therefore is quieted more readily than in night terror. Thus we see also in children anxious dreams leading to various degrees and kinds of manifestations; the more violent forms especially in nervous or lively natures. Screaming in fever is not rare even among otherwise healthy children.

Pavor nocturnus, if occurring at long intervals, especially if accompanied by enuresis nocturna and followed by a prolonged dazed condition, should arouse the suspicion of an epileptic basis, as we observe epileptic attacks of this character also in the adult.

That exogenic stimuli, as noises, light, etc., during sleep do influence the content of dream ideas, everybody's self-observation will reveal and has been demonstrated experimentally; the sensory stimulus, however, undergoing various, often fantastic interpretations. For instance, exposure by pushing off the cover, with a feeling of chill, may create the embarrassing dream situation of finding oneself disrobed on the street, or the chilly feeling will be interpreted in the dream as due to a cold wind while preparing for a bath in the open. This is also true as to somatic processes; for example, the peristalsis of intestines, full bladder, distress of heart, etc. Extraneous and somatic factors of a disagreeable sort may thus cause disagreeable dreams with or without awakening. The weight of the incumbent arm and its mechanical pressure on the chest, or sleeping on the abdomen, may provoke some fear dream, as, for instance, the well known incubus, with dyspnea, distressing feeling of oppression, as if an animal were sitting on the chest, or the feeling of being paralyzed and completely helpless. Pain in the limbs from whatever cause may be magnified to an actual laceration by wild animals; a violent neuralgia in the adult may lead to a dream sensation of being stabbed by a dagger, and become the peripheral stimulus for a dream phantasma, in which through associative processes, for instance, thoughts of a murderer, of fight, of danger to life, will ensue. Chronic diseases with organ sensations may lead to the recurrence of the same dream (*Wiederholungsträume*).

A 12 year old boy patient of Henoch (quoted from Soltmann) suffering from tuberculous spondylitis had night terrors, always connected with the feeling of an animal sitting on his back and pressing him.

A girl of 8, admitted to the Cook County Hospital with mitral affection and severely decompensated heart was for several nights during the last weeks before death found screaming in fear and crouching behind the back rest, whither she had crawled, though otherwise being unable to move on account of orthopnea. Questions asked were answered correctly, but she did not know the cause of her fear nor how she happened to be behind the back rest.

It is probable, a fearful dream was provoked by oppression in the heart region, creating fear hallucinations; she then acted in a twilight state of half sleep, from which she was easily aroused, but with complete amnesia.

Hypnalgias and allied oneirogenic disturbances.—Of an oneirogenic basis, similar to pavor nocturnus, but without the element of terror, are those peculiar disturbances, as whining, moaning and complaining almost exclusively during the sleep of abdominal pain, or the occurrence of attacks of vomiting or coughing without awakening that yield to simple suggestive therapy (psychotherapy), thus evidencing their psychogenic origin (Hamburger). A case of such oneirogenic gastralgia and vomiting occurring only during sleep and causing awakening was published by me in this journal.[8] Also in this case the definite disappearance of the nocturnal attacks for which no organic cause could be detected, on a merely suggestive medication with verbal assurance of cure, brought forth into clear view the psychogenic element of this disorder.

Oppenheim has called attention to the relation between certain pains, the so-called hypnalgias and the processes of sleep. A number of his patients, adults, had suffered from cardialgias or neuralgias that aroused them from sleep and persisted only a short time after awakening, appearing again, however, as soon as they yielded to the desire for sleep. In a number of these cases the origin of the disturbance in the view of Oppenheim was probably pain hallucinations, which, like other sensory illusions, are in connection with dreams. In others the manifestations had probably a relationship to the processes of sleep themselves, the altered function of the nervous elements of the brain, its anemia, etc., which, as known, not infrequently create in certain epileptics conditions for nocturnal attacks. Some symptoms, as anxiety, attacks of pain and paresthesias may exacerbate during the night, because the patient gives more attention to his somatic processes; perhaps also due to the abrogation of the influence of the higher nerve centers.

Insomnia.—Insomnia may be transitory or persistent. Though it may have its causes in some organic trouble that has been dealt with before, instances without it occur in childhood, even in infancy, in great numbers and are often very obstinate. The objective examination and further observation will reveal a nervous constitution, the insomnia being only one of several evidences and symptoms of this anomaly. The disturbance may manifest itself at the period of falling asleep, or during the sleep proper, or at both periods. In the first case the children, infants as well as older ones, do not fall asleep as

8. Strauch, A.: Am. J. Dis. Child. **16**:165, 1918.

rapidly as normally after satiation or when put to bed, but lie awake even for hours; the ensuing sleep will be normal, deep and long. No significance will be ascribed to older children who represent the "morning type" remaining awake late in the evening, fresh and efficient; but it is pathologic, if children who have all signs of weariness, fatigue, sleepiness and desire for rest, cannot find the latter and lie wide awake with open eyes, often anxious and restless. In other cases the individuals fall asleep promptly, but the quality of the ensuing sleep is defective, shallow, readily disturbed and interrupted by slight noises or light, or even without recognizable external causes; there may be shorter or longer periods of wakefulness, during which the children may ask for this or that and disturb the whole household. This is abnormal, since the sleep of healthy children is comparatively sound, and infants are not easily disturbed by the ordinary amusements of their sisters and brothers; and often children who fall asleep on the chair can without awakening be undressed and carried to bed. No doubt, in a number of these cases some minor somatic disturbance may lessen the depth of sleep and thus render them more easily awakened. In still other instances the children merely wake too early in the morning and find no more sleep; or there may be combinations of these disorders in the various periods of sleep.

Environmental factors.—Appreciating the neuropathic factor in these cases, nevertheless the sleeplessness will not infrequently find its explanation perhaps rather in psychic and pedagogic errors of the environment than in the child itself. Perverted education all too often permits excitement of the child's phantasy by too intense play, by exciting tales or too absorbing reading immediately before going to bed; also allowing too late hours will retard sleep. The relation of kino-performances and child psyche should here be emphasized, especially in nervous, excitable, predisposed individuals, as the former may have untoward effects on the health, creating fears, states of anxiety and vivid, violent dreams, and so sleeplessness. Even films not objectionable from an ethical-moral standpoint may influence most unhygienically the easily aroused imagination, since sentiments and emotions play a great rôle with the child, not to mention sexual stimulation. Fear need not assume a clear idea or image; it may be indefinite. Also agreeable promises may excite a child, as it is a well known fact that the anticipation of a pleasure, for instance on the eve of excursions, pleasure trips, awarding of school honors, etc., will interfere with good sleep.

Intimidation, threatening with the black man, etc., injuries suffered, exciting scenes of the home life, school fears, physical discomfort, may disquiet the child and fill it with anxious dreams and sensations;

especially with abnormally timid and irritable individuals will such states of fear and various phobias play a great rôle. The young victim may have difficulty in falling asleep or will wake up with a heavy feeling of dread and afterwards spend the night for a period restlessly, controlled by this emotion. The sufferer might then even refuse to go to bed at night out of fearful anticipation of such dream images and phantasms.

A 2 year old, perfectly healthy boy, of a sudden showed great fear when taken to bed one night, clinging to his mother, struggling violently when being laid down, and crying and screaming for half an hour, until he fell asleep from mere exhaustion. Such vehement fear paroxysms occurred thereafter not only at bedtime at night but also at naptime, until the affection finally wore off in a week. Only touching his mother would eventually render him restful; other means, such as sitting of his mother in the room, burning a light, chastisement, etc., were of no avail. After the subsidence of these attacks the child still showed fear for a while even in daylight at finding himself in a room alone. The only explanation for this being afraid of going to bed was frightening dreams following a heavy thanksgiving supper and unusual excitement the night before the fear attacks started.

In other instances children out of fear to sleep alone will permanently ask for this or that or for an adult person to sit at the bedside, but then will distrustfully open their eyes time and again to see whether the person is still present. Instinctive, indefinite fear of darkness may, especially in nervous children, prevent or otherwise disturb sleep.

Sexual factors.—According to Stekel,[9] children who manifest signs of fear neurosis, have in some way come in contact with the sexual problem; the not understood, not gratified libido, sexual stimulation and suppressed sexual excitement have from subconsciousness or unconsciousness risen into consciousness in the form of anxiety or fear sensations. In his experience exaggerated tenderness, permanent unnatural caressing or negligence on the part of the parents, kissing, hugging, sleeping with the loved person in the same bed, especially of the other sex, but also of the same sex, may call forth prematurely the first erotic instinct and sensation in the child, which is far from being asexual, but, according to Freud, rather "polymorph perverse." Among a number of cases instanced to prove his statement, a boy refused to sleep, because he wanted to watch the undressing of his governess. In his cases the resulting sleep disturbances were promptly cured by complete separation. His observations suggested sexual stimuli by an attending person through unintentional irritations by caressing, kissing and undressing before the child; in other cases, direct sexual traumas, as acts of masturbation. The following case of mutual and solitary masturbation came to my notice the past summer:

9. Stekel: Med. Klin., 1908, p. 621.

A boy of 4½ years was observed to practice manual masturbation several times a day and also at night before falling asleep. His 2½ year old brother, who slept in the same bed, did not fall asleep one night, cried much and fussed until 2 o'clock in the morning. When urged to tell the cause of his behavior, he demonstrated the sexual practices of his older brother on himself and said the latter "had not yet done this to him this night as before."

Though we can not follow Stekel's ultraradicalism in his overemphasizing the sexual element in sleep disturbances in children due to anxiety neurosis, tracing every pavor nocturnus, every chronic sleeplessness to some sexual basis, such possibilities and facts as he instances must be acknowledged to occur, perhaps more frequently than is generally thought. His reported cases carry a strong conviction with them, though I am sure they are rather the exception. In obscure cases we should follow this trend of evidence in our investigation of the etiology of the individual case. That hugging of a beloved mother by the boy or stormy manifestations of affection by the mother may indeed arouse some reactive sensations in the child was brought to my notice again a short time ago by an overindulgent mother who reported that her 4 year old boy when hugging her repeatedly had manifested erection.

That irrational, excessive fondling and nervous behavior of the mother may contribute to sleeplessness, apart from sexual factors, is also shown in the case reported by B. Sachs in his textbook on nervous diseases of children, where the mother used to take the awakened child into her own bed and by caressing and despair over its not sleeping, would excite the child the more, making matters worse and worse, until a trained nurse was taken.

A similar case came to my observation recently.

The nervous mother, wife of a physician, admitted having made herself a slave to her 22 months old daughter. Not only had she to rock the very nervous baby to sleep, but she would, at the slightest whimpering, take her up, fondle and excite her, until the child would rather regularly awake about midnight and cry for as much as two or three hours and tryannize the household; only if rocked would she fall into a very superficial, interrupted slumber. A nurse was employed for two weeks, when the sleep at once became satisfactory, but the former trouble started anew when the mother again took charge of her child.

A 4 year old child of a physician, who sleeps extremely superficially, being disturbed, for instance even by his mother most cautiously entering his room, would, at the age of 2 years, regularly awake during the night, begin to babble and then, apparently without cause, burst forth in a paroxysm of loud, continuous laughter; this would last about one hour and by its violent and forced character had, in the view of the mother, assumed disquieting, well-nigh alarming character, as if foreboding "some mental disturbance." Then, tired out by the paroxysm, the child would cry and shriek for another hour and finally fall asleep from mere exhaustion. The disturbance lasted several months, but has lately occurred only on two occasions during attacks of tonsillitis.

There can be no doubt that sexual habits in older children actually may banish sleep, the children keeping themselves awake or half awake in order to gratify masturbatory tendencies, as such acts are, especially at night in the solitude of the bed, undisturbed by the possible observation of guardians. Such sleeplessness is intended. Or with the age approaching puberty, psychic masturbation, that is to say, the indulgence in sexual phantasies, in voluptuous pictures and erotic ideas may be encountered as a cause of delayed sleep. On the other hand, real masturbation may result possibly from simple playing with the genitals, incited by the ennui and tedium of wakefulness itself. Since the act of masturbation often is followed by marked fatigue and exhaustion, as also normal coitus in the adult promotes sleep, it is asserted by good authorities (Heller[10]) that psychopathic sleepless children and youths may masturbate not merely for gratification, but also out of intense desire for sleep.

DIFFICULT AWAKENING, INCREASED REQUIREMENTS OF SLEEP

As falling asleep, so, vice versa, the process of awakening may be difficult. Nervous children are often, even after a long night's rest, still sleeping in the morning, do not want to get up, are peevish if aroused, and dress and breakfast in a sort of half-sleep that only slowly disappears. They are not refreshed, but on the contrary feel tired, are irritable to the extent that insignificant provocations cause excitement. Such children may show in the morning a wilted expression that suggests a nonrefreshing night's rest. Most nervous, but also some nonnervous, children represent the "morning type," of which mention was made in a former paragraph. For them, of course, the too early beginning of school work is not to be recommended even with early retiring; particularly does the shortening of the morning sleep postpone the maximum of efficiency in their day's work. This type is, of course, to be judged in a different way from that in which children, on account of late hours, through wrong education, or on acount of some sleep trouble have not had sufficient sleep in the morning.

An abnormal requirement and profundity of sleep is to be observed in normal children in exhaustion as the result of too great expenditure of energy, and also among cretins and in hypothyroidism. Easily exhausted, nervous children may need an amount of sleep far in excess of the ordinary, and they occasionally manifest a marked desire to sleep during the day, falling asleep at any time, even up to the age of 12 or 14, whereas healthy children from the third or fourth year

10. Heller, Th.: Heilpaedagogik, Ed. 2, Leipzig, 1912, p. 452.

will object to the afternoon sleep, preferring instead to pursue interestedly their play throughout the day.

In a few extreme cases children reverse day and night in the distribution of their sleeping hours, as in the observation of Baginsky, where a girl of 5 years, suffering from permanent fatigue and discontent, "turned the night into day, and vice versa." No sleep could be obtained in the night, which was passed in singing, playing, eating, etc.; only during the day would she sleep. A cure was effected in two weeks by change of environment and through strict discipline by an intelligent nurse.

A very profound and fast sleep — be it due to overfatigue or not—is met with in children who suffer from enuresis nocturna. It is noteworthy that the bedwetting mostly takes place in the second or third hour; that is, at the period of deepest sleep. We frequently hear from the parents that loud noises, as the ringing of the doorbell, rapping at the door, etc., do not disturb the child, while the rest of the family are aroused, and it is difficult in such case to awaken the bedwetter in order to have him urinate. In a number of instances the patient, even after shaking vigorously or sprinkling with cold water, would urinate only in a dazed state, in which he would stray confusedly about, not being able to find his bed; yet he may, as I have seen, wet the bed only fifteen or twenty minutes later, having rapidly fallen again into the profoundest sleep. Such children also in the morning are frequently difficult to arouse. A girl of 2½, who not only suffered from enuresis nocturna, but manifested also other nervous disturbances, as tossing and loud habitual screaming in deepest sleep, was not awakened by violent slapping on the hands, though shrieking was stopped for a while.

The attacks of sleeplike, lethargic states, sometimes observed in epileptics and older hysteric children which occur with or without connection with paroxysms should not be discussed here at length, since they belong to the psychic disturbances of these diseases. The transition from the waking to the hysterical sleeplike state takes place, as a rule, rapidly, in some cases more gradually, and its duration may extend from hours to days and even weeks or months (hysteric pseudodeath). A case in which the epileptic attacks consisted exclusively of sleep with sudden onset was described by Ulrich (quoted from Th. Heller, p. 80).

TREATMENT

Sleep disturbances in children, as a rule, are easily and readily influenced therapeutically. Before beginning treatment the somatic causes, if any, must, of course, first be made out and alleviated; the possible lack of comfort and hygiene and other disturbing extraneous

circumstances enumerated before must be considered. The sleep should not be disturbed except for good reasons. Many habits of the nursery, as singing or rocking to sleep, giving unwarrantedly water or milk during the night, too late retiring, taking up the child as soon as he utters the first cry, too much fondling, must be avoided. Irritation, overstimulation of the imagination and provocation of emotions, especially of fear and anxiety, must be avoided, as likewise other errors in education and management.

The more certain it is that fear-affects interfere with sleep, the more must we make efforts to free the victim of them by removing the psychic sources. It would be cruel not to alleviate dread. It may be necessary to keep the door open, so the child will know that a person is near by, or to keep a light burning low, to be turned down soon, of course, and extinguished finally, until in a few days, as a rule, the child will fall asleep alone in the dark room. Suasion by calming words and other suggestive means should be employed by the mother, as sitting at the child's bedside, placing the hand on its head, stroking, offering a glassful of water, etc. Under these circumstances, however, the possibility must be kept in mind of decreasing the profundity of sleep by a strong light, or of the patient acquiring a new sleep disturbing habit, wanting to be treated always in this way.

Suggestion employed in the waking state has a decided influence on a number of sleep habits and disturbances, in the same manner as on psychogenic disorders manifested during the day.

Many recurring sleep disorders are habits with associations of psychogenic reflexes (pavor, somnambulism, enuresis, etc.). Once the first member of these associations is reproduced, the rest will automatically ensue as a reflex, assuming the type of simple or more complex somatic and psychic processes. The curative mechanism of suggestion lies in the fact that, if the first mental process, the stereotyped provocative conscious or unconscious "memory" is prevented from springing forth, also the supervening psychic reflexes will fail to take place.

An alteration of the psychic life, as, for instance, by change of environment, by transfer to relatives, or especially to a hospital, even a mere threat of it, the separation of the child from the overindulging mother, introduction of a new nurse with disciplining talent, even a mere change of the bedroom will contribute much to influence and abolish entirely those mental complexes that, particularly in children, return in a stereotyped manner before sleep overcomes them. With the former conditions altered as indicated, the child takes entirely new and different ideas into his dream life; and even should the suggestive means fail to prevent entirely the "starting idea," nevertheless it will

block and inhibit the otherwise ensuing morbid psychoreflectoric complex by diverting the associations in another direction. These extraneous changes, though some of them may seem insignificant to the mind of the adult, will frequently bring about a cure within a few nights of insomnia, pavor nocturnus, enuresis and various other sleep disturbances. This fact also explains the rarity in hospital practice of the occurrence of certain disorders of sleep, as pavor, somnambulism, wakefulness with asking questions, desiring this and that during the night, etc. Promises of reward, threat and punishment, if necessary, will be of aid to the child, as the removing or returning of some favorite plaything. An intelligent, energetic nurse or attendant will work wonders in the home. Also the faradic current is a powerful suggestive means, though rarely necessary.

If in habitual insomnia other therapeutic means are indicated, prolonged, warm, full baths or foot baths, or lukewarm hydropathic packs of body or legs will often be effective. In temporary sleeplessness due to exhausting acute diseases with an urgent indication to induce sleep, as in restlessness of infants from nutritional disturbances with colic pains, or in highly febrile diseases, as typhoid, we should not hesitate to administer drugs until their physiologic effect is established, such as chloralhydrate, bromids, trional, sulfonal or veronal. In the chronic forms of insomnia these drugs are only exceptionally, at most only temporarily, to be prescribed, and then, as soon as possible, discontinued or replaced by pharmacodynamically mild or even indifferent medicines. The latter, as tincture of valerian, are relied on not so much for their physiologic effect as for their suggestive element, masking the principle of psychotherapy in older children. Therefore, they should be given immediately before retiring, accompanied by a strong verbal suggestion of effectiveness, as by the words, "Take the medicine; it will make you sleep" (Hamburger). The assurance of cure is important for the effect of psychotherapy, in order to make a deep impression on the child's mind.

In exceptionally persistent cases, a radical change of the *milieu* by transfer to a hospital may be necessary. In combating the symptom let us never overlook the treatment of the underlying nervous diathesis by general hygienic and pedagogic measures.

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PROGRESS IN PEDIATRICS

A REVIEW OF THE LITERATURE OF THE PAST YEAR (1918) ON GENITO-URINARY DISEASES IN CHILDREN

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BACTERIOLOGY OF THE URINE

Schwartz[1] investigated the bacteriology of the urine of children with gastro-intestinal disease, and found that urethral and bladder contamination was very common. This was particularly true of girls, which favors the theory of ascending infection in pyelitis. In sixty-three infants with various gastro-intestinal disturbances, thirty-eight, or 60.3 per cent., showed the presence of gram-negative bacilli in the urine. Of those in which the first and second portions of the urine were separately cultured, 21.4 per cent. showed a sufficient number of gram-negative bacilli in the second specimen to constitute a bacilluria. Urethral contamination was almost three times as common in girl babies as in boys, while actual bacilluria was twice as prevalent in girls as in boys.

ALKAPTONURIA

Schochet[2] discusses alkaptonuria. About seventy cases of alkaptonuria have been reported in the literature. The term "alkaptonuria" was first introduced by Bodeker in 1857 to describe a substance found in the urine, which possessed two chief characteristics: first, the power to reduce alkaline copper solutions, and secondly, the property of absorbing oxygen from the air in the presence of alkali, and as a result turning to a brown black color. The urine may be clear and a normal color when passed, but later becomes dark brown or finally black on exposure to the air. There is no treatment for the condition, and it is of no pathologic significance. It is important, however, in that it may be mistaken for glycosuria. Negative results with fermentation and the polariscope should at once rule out glycosuria. Alkaptonuria must be differentiated from the hemoglobinurias due to drugs (phenol) and diseases (malaria) by the presence of hemoglobin in the urine; from the melanurias and hematoporphynurias,

1. Arch. Pediat., January, 1918.
2. Arch. Int. Med. **22**:82, 1918.

and from the condition known as "paroxysmal hemoglobinuria" by chemical and spectroscopic tests for the pigments.

RENAL GLYCOSURIA

This interesting condition is discussed in two exhaustive papers by Beard and Grave[3] and by Goto.[4] Beard and Grave say that the condition should not be called "renal diabetes" but "renal glycosuria," as it has nothing to do with true diabetes. It is a very rare condition, and many cases so diagnosed are in reality mild or typical cases of diabetes mellitus. The lesion is renal, and is manifested by a constant excretion of a small amount of dextrose by the kidney. The blood sugar is normal. The tissues can still utilize carbohydrate—on any diet the percentage of sugar does not vary greatly. Most of the patients are apparently in good health. In order to make a diagnosis of renal glycosuria it is necessary to have the following data: (1) a urine containing dextrose, the amount of which is unchanged to any great extent by variation of the carbohydrate intake; (2) a normal blood sugar. (May vary normally between 0.7 and 0.15 per cent.)

Goto[4] writes as follows:

The general conception now is that anatomic change in the kidney is not necessary for the occurrence of renal glycosuria. The reasons for the permeability of the kidney to sugar are not known.

Since we know that the blood sugar undergoes marked and rapid fluctuation after the ingestion of carbohydrate and that urinary sugar has some relationship to hyperglycemia after meals, it is hardly possible to deny, to a certain extent, at least, the existence of a relationship of urinary sugar in renal glycosuria to the carbohydrate content of the diet. In the case reported by Goto there was no urinary sugar when the carbohydrate in the diet was below 34 gm., because the alimentary hyperglycermia occurring with that diet is under the threshold of the kidney for sugar. The blood sugar was highest after 200 gm. of glucose, but the urinary glucose in that case was less after 100 gm. glucose. Renal glycosuria may depend to a certain extent on the carbohydrate content of the diet:

1. When the renal permeability is but slightly affected, glycosuria may not appear after a carbohydrate poor diet, but when it is severely affected, glycosuria will not disappear even after the entire withdrawal of carbohydrate from the diet.

2. Urinary sugar is not excreted proportionally to the increase or decrease of carbohydrate in the diet. The most important point in the diagnosis of renal glycosuria is the presence of the normal level of

3. Arch. Int. Med. **21**:705, 1918.
4. Arch. Int. Med. **22**:96, 1918.

blood sugar, when sugar appears in the urine. During a long period of time there is apparently, in the few cases reported, no tendency for the amount of sugar in the urine to increase — the patients seem perfectly well, and the condition is usually found during a routine urine examination. No treatment is necessary, and there is no use of decreasing the amount of carbohydrate in the diet, as this is without effect on the glycosuria.

ENURESIS

The literature on enuresis is always interesting, as no two authors use the same methods of treatment. Enuresis is a rather complex condition, which may be a resultant of many causes, and hence the good results reported by different observers with totally different methods of treatment. Many drugs have been used in the treatment of enuresis, some with apparent good results, but it is certain that in any condition where many drugs have been used, no drug is of specific benefit. We believe (see following) at the Children's Hospital that an intelligent regulation of the child's daily life, nervous system, diet, etc., is of more importance than drugs, and Dr. Grover has had excellent results in many cases without using a drug of any sort (see following).

Neave[5] recommends making the child sit on its chair and hold its water when it wishes to micturate, thus gradually teaching it control.

Fisher[5] has had good results with sulphonal. He gives 1 grain for each year of the child's age every night for the first week, every other night for the second week, and every third night for the third week. In a considerable number of cases, after this routine has been followed for three weeks the child is permanently cured.

Thompson[6] has had good results with a widely different method. He inserts a catheter in the bladder, and runs in fluid at a low pressure. At first only that amount of fluid which the patient can hold with comfort (about 3 ounces) is inserted. The fluid injection is repeated three or four times at short intervals, with gradually increasing amounts of fluid. The treatment is carried on for ten days or so until about 10 ounces of fluid can be retained. The fluid used is boric acid solution at a temperature of 100 F. The essential points in the treatment are: (1) passage of a clean catheter; (2) ingestion of gradually increasing quantities, by which the bladder is slowly trained to hold more fluid than it has previously held.

Emerson[7] reports thirty-four cases of enuresis treated successfully without drugs. Enuresis in children is not a disease, but simply the

5. Lancet, London **2**:728, 1917.
6. Lancet, London **2**:623, 1917.
7. Am. J. Dis. Child. **15**:339, 1918.

persistence of an infantile condition, or habit. Innumerable conditions have been cited as the cause of enuresis, but from their very multiplicity it is evident that the true cause has not been found. In a group study of 100 children reported by Emerson, no special incidence of enuresis was found with adherent prepuce or clitoris, mental retardation, carious teeth or malnutrition. There was, however, marked incidence with nasopharyngeal obstruction. The treatment may be considered to consist of four methods, all or one of which may be used in a given case to establish the "dry habit." The "dry habit" once started must then be continued by careful oversight.

First Method. — Mental suggestion. By arousing the patient's desire to be dry by rewards and other mental suggestions, this is entirely adequate to relieve about 40 per cent. of all cases of enuresis.

Second Method.—By teaching the child to urinate before he wets himself, the urine being voided at regular intervals, and the time between intervals being gradually increased. By such training the act of urination soon comes under the patient's control.

Third Method.—Local irritation. This consists in irritating the vesicular sphincter and the posterior urethra by a bougie-a-boule, so that sensory impulses passing to the brain will become intensified sufficiently to attract the patient's attention, until the habit of control is attained. The bougie is introduced into the bladder, withdrawn, and then passed in and out about four times, enough to cause a sensation of discomfort during the next few urinations. This sensation of discomfort in urinating brings the act into the child's consciousness, aiding him in control.

Fourth Method.—Cerebrospinal irritation. This is produced by the injection into the spinal canal of physiologic sodium chlorid solution, producing such stimulation as to arouse the whole mechanism into consciousness, when habit holds it under control. Ten c.c. of spinal fluid are withdrawn, and 12 c.c. of normal saline introduced. This method is necessary only in extreme cases of enuresis, or in those complicated by mental deficiency, and should be used only after other methods fail.

Grover[8] has made a study of bed wetting and clothes wetting in a series of 200 cases in the outpatient department of the Children's Hospital, Boston. The ages ranged from 4 to 12 years. He found a history of enuresis in the immediate family in 56 per cent. of the cases. Although adhesions of the prepuce, adenoids, worms and high acidity or alkalinity of the urine are usually considered as of prime importance in the etiology of this disease, Grover has disregarded them and has

8. J. A. M. A. **71**:626, 1918.

acted on the assumption that enuresis is due to what he terms a "general fatigue" of a neuromuscular nature. This fatigue is brought about by too much exercise, too little sleep, and more especially by an irregular and poorly chosen diet. After the condition has been going on for several months, a habit of involuntary wetting is acquired, which may persist long after the neuromuscular fatigue is overcome. His treatment is along hygienic and dietetic lines, no drugs of any sort or mechanical or operative means being used.

The child is put to bed at exactly 7 p. m., after urinating. He is then waked at exactly 10 p. m. and 6 a. m. to empty the bladder. In the very active children, an additional rest hour is provided immediately after the noon meal. No exercise is allowed after 4 p. m. Music lessons, moving picture shows, etc., are prohibited. The diet excludes candy, cake, ice cream, soda water, cookies, chocolate, jams, jellies, syrups, coffee, tea, cocoa, meat broths, raw apples, bananas, condiments, pickled and salt foods, frankforts, baked beans and eggnogs. Meat and vegetables are prohibited at night, and no food of any description is allowed between meals.

The habit of wetting is taken care of by limiting all fluids after 4 p. m., and by the regular urinations at 7 p. m., 10 p. m. and 6 a. m. The habit of clothes wetting and frequent micturition in the daytime is treated by having the patient pass water every ten or fifteen minutes right through the day. This interval is lengthened by five or ten minutes every week, until the interval is two and a half hours. A large percentage of patients were cured in from one to thirty days. A conscientious mother, and an obedient, interested child predispose to a rapid cure. The hygienic and dietary measures outlined not only help the enuresis, but also relieve the nervousness and habit-spasms that so often accompany the condition.

CALCULUS, PYONEPHROSIS, ETC.

Tuberculous Obstruction.—Thompson[9] in a discussion of the surgical aspects of genito-urinary disease in children, says that occasionally tuberculous peritonitis may be a cause of urinary symptoms by causing a constriction of the ureter, which may bring about symptoms of renal colic. The child is brought in with a history of severe radiating pain in one loin and occasional hematuria. Roentgenograms may reveal a shadow in the region of the upper urinary tract, which suggests stone. An exploratory operation is performed, and no stone found. In such cases a very careful examination of the ureter should be made, and not infrequently it will be found that there are peritoneal bands binding the ureter down to the posterior abdominal

9. Brit. J. Dis. Child, April-June **15**:6, 1918.

wall, or even kinking it, or there may be a small mass of tuberculous glands pressing on the ureter and leading to obstruction. In the Guy's Hospital necropsy reports there were found twenty cases of tuberculous peritonitis in which there was evidence of obstructive conditions in the ureter. Cystoscopy, the passage of a ureteral catheter, and the injection of some opaque material into the pelvis of the kidney, with roentgen-ray examination, should enable a diagnosis to be made between a calculus situated within the upper urinary tract and tuberculous glands, producing pressure on the ureter from without.

Pyonephrosis.—This may occur from calculus or from aberrant vessels. Calculi may occur at an early age. For the ultimate cause of their formation we may have to go back to very early life. From many autopsies at Guy's Hospital the following is apparent: in the pelvis, and in the kidney substance, uric acid, sand, concretions or even very small calculi may be found after death from marasmus, or an acute infectious disease with which considerable wasting has been associated. It is not unreasonable to assume that these concretions may be the origin of larger stones and may bring about the formation of definite calculi. It is important to note that in children the symptoms of renal stone may occur on the side which is not affected.

Collins[10] discusses the diagnosis of renal stone in infants and children. At first the child may simply cry a little on urinating, when no external evidences of irritation are visible. Frequency of urination is likely to occur. As the trouble progresses bladder pain becomes evident, especially when the child is active. Greater pain on urination, leading to tenesmus and rectal prolapse, may occur. Sudden cessation of the urine flow may be a common symptom in some cases.

PYELITIS

Helmholz[11] reports three cases of pyelitis in the new-born; all were boys; all showed the colon bacillus in pure culture. The most effective treatment was found to be 5 grains of sodium bicarbonate with 5 grains of sodium citrate every three hours.

In another paper Helmholz[12] discusses pyelitis. Pyelitis is characterized by the absence of local and the presence of general symptoms. General symptoms are chills, fever, pallor, loss of appetite and prostration. The younger the child the less likelihood there is of being local symptoms. The infrequency of local symptoms makes it absolutely essential to examine the urine repeatedly in any obscure febrile condition in infancy and childhood. Pyelitis frequently com-

10. Arch. Diag. **10**:259, 1917.
11. Med. Clin. N. Am. March, 1918.
12. Illinois M. J. **32**:311, 1917.

plicates acute infections and gastro-intestinal disturbance, and also gastro-intestinal disturbances frequently occur secondary to pyelitis, and are wrongly considered the sole cause of the fever. One must distinguish between primary and secondary forms of pyelitis.

In the first, the illness begins acutely in a child that is perfectly well; the child suddenly becomes sick with high fever and an absence of physical signs.

The second form may develop during a gastro-intestinal disturbance (summer type) or after infections of the upper respiratory tract (winter type). As a result of temporary plugging of a ureter, the pus may disappear from the urine for from twelve to twenty-four hours. The variability of the clinical picture is such that the only manifestation may be a slight fever, or again, the picture may be so severe as to suggest an acute meningitis. Severe complications are usually due to involvement of the kidney substance. There is a marked tendency to recurrence. The most important single point in the therapy of pyelitis is the free administration of liquid. In the drug treatment we must differentiate between the infant and the older child. The infant usually does best on the alkaline treatment. To an infant of 2 months or over, 90 grains of potassium citrate may be given every twenty-four hours, and this may be increased by 60 grains every day until the urine is alkaline. The urine must be kept alkaline at least two weeks.

It is doubtful exactly what the action of potassium citrate is. It has no antiseptic effect; the bacteria are just as numerous in the alkaline as in the acid urine (?)—although the clinical symptoms have gone. It appears, therefore, that the action of the citrate is largely a diuretic one. If the acid treatment is to be used, from 3 to 5 grains of hexamethylenamin four or five times in the twenty-four hours may be given to a child over 6 months old. If plenty of fluid is given, the danger of producing hematuria is very slight. In older children the potassium citrate treatment is often ineffectual, so that if after three days of treatment the child is no better, it is better to change to hexamethylenamin.

R. M. Smith[13] says that pyelitis is a common disease, and comprises 1 per cent. of all cases seen. The youngest case he has seen was in a boy 2 days old. After the fourth month it is more common in girls; before this the incidence is about equal. It may begin with gastro-intestinal symptoms such as vomiting and diarrhea, which may mask the real trouble. Urinary symptoms are usually slight or absent. In 75 per cent. of all cases colon bacilli are found. The course is variable, but in general, children with acute and severe symptoms

13. Med. Clin. N. Am. **1**:1165, 1918.

do better than those with a less vigorous onset. The tendency is to become chronic, and relapses are frequent. The blood is the most probable source of infection. The probable course is somewhat as follows: the organisms enter the blood from the intestinal tract or other parts of the body. Entering the blood directly or through the intermediary lymphatic route, they pass with the blood into the kidney through the glomeruli, down the tubules and out at the pelvis. During the passage through the kidney they may or may not cause an infection. What happens depends on the virulence of the bacteria and on the general resistance of the patient, and the local resistance of the kidney. Colon bacilli have a low pathogenicity; therefore, they rarely cause infection in the kidney. In being excreted at the pelvis, an inflammatory process, causing the disease pyelitis, occurs. There may be an infection of the kidney by extension inward from the pelvis via the lymphatics, but it is not directly associated with the primary condition. A large amount of experimental evidence has been collected to substantiate this mode of infection, and all the various steps in the process have been shown possible of occurrence.

NEPHRITIS

Etiology and Classification.—Ophüls[14] believes that lesions of the glomeruli play a most important part in nephritis and often form the one connecting link in a "bewildering multiplicity of other developments."

"The differences that have been so carefully studied by the pathologists and have given rise to our complex and often confusing nomenclature, naturally remain, but as purely descriptive subdivisions. They should be relegated to that point of relative importance to which they may still lay claim, and should not be permitted to cloud the real picture by the introduction of a mass of perhaps interesting, but evidently subsidiary detail."

It is very likely that the glomerular lesions are embolic, and due to the rapid lysis of the bacteria within the vascular loop of the glomeruli. Streptococci are by far the most common organism concerned in nephritis. The most dangerous forms of nephritis are those associated with streptococcic infections of the tonsil, in which cases the persistence and recrudescences of the renal disease are probably due to the persistence of a septic focus in this locality.

Ophüls recognizes the following groups of nephritic cases due to streptococcic infection:

1. *Acute Glomerulonephritis.*—This is usually due to some septic infection. The glomeruli are intensely inflamed, permitting the escape

14. J. A. M. A. **69**:1223, 1917.

of blood, albumin and leukocytes into the capsular space and the tubules. There may be a moderate or a very large amount of blood in the urine. There may or may not be edema.

2. *Subacute.*—This may develop insidiously, and it may be impossible to ascertain the date of onset. The necrotic spots in the diseased glomeruli gradually become replaced by connective tissue, which eventually destroys the glomeruli entirely and converts them into inert masses of fibrous connective tissue. In some cases the blood vessels begin to develop serious lesions. Sometimes these patients are well for a long time, and the condition is discovered only accidentally, or in the last stages, when severe symptoms begin to arise.

3. *Chronic Form.*—In eight cases investigated there was chronic disease of the tonsils, with multiple pus pockets. The tonsil condition may be present without any knowledge on the part of the patient, and is difficult to discover clinically. Why such a condition, which is common in many people who do not have nephritis, should cause nephritis in some persons and not in others is hard to explain. The development of the chronic cases is very insidious, and the course extends over many years. The original lesion in many of them undoubtedly dates back to childhood. The clinical history usually begins only a few months, or at best a few years, before death, when there is often quite a sudden change for the worse from a condition of apparent well-being. The kidneys at necropsy are always much shrunken and show the characteristic microscopic picture of an advanced renal sclerosis. "The patients in this last group vary so much in their rate of development, in the gross and microscopic appearance of the kidneys, and in their symptomatology, that one can readily understand why, both from an anatomic and a clinical point of view, numerous efforts have been made to subdivide this group into subgroups according to whether the disease of the blood vessels in the kidneys plays an important rôle, or whether clinically the signs of cardiovascular disturbance predominate over those of renal origin, or vice versa." Such a subdivision does not seem feasible.

SUMMARY

"1. There is a well defined disease of the kidneys caused by general sepsis arising from some infected focus, and often made progressive by the persistence of such a focus.

"2. Since the glomeruli in this disease show the most characteristic and constant lesions we may speak of it as glomerulonephritis, and as the lesions are so distinctly of an inflammatory character, as true nephritis.

"3. The disease occurs in three forms; acute, subacute and chronic.

"4. Characteristic glomerular lesions may be produced in animals by injection of bacteria into the blood stream.

"5. Many of the chronic cases seem to be caused by a peculiar form of chronic suppurative tonsillitis due to diplostreptococcic infection."

Stengel[15] discusses the classification of nephritis.

The pathologic changes in damaged kidneys may be grouped under three heads:

1. Glomerular change, which may present itself as hemorrhage or exudation in the space between the capillary tuft and the outer limiting epithelial lining of the sac, proliferation and degeneration of the epithelia, hyalinization, atrophy or sclerosis of the malpighian body, thrombosis of the capillaries of the tuft, and in later stages sclerotic thickening of the outer wall of the capsule.

2. Tubular changes, manifested by swelling and degeneration of the epithelial cells lining the tubules.

3. Sclerosis in the form of concentric layers of fibrous tissue surrounding the diseased malpighian bodies, or as fibrous thickening and condensation of the intertubular tissues, is a late result of either the first or second group of changes.

"It is obvious that in a complicated glandular structure such as the kidney, a pathologic lesion is not likely to confine itself to one of the histologic elements to the exclusion of the adjacent parts, and clinico-pathologic experience shows that combinations occur in renal diseass which make a rigid classification of definite forms untrustworthy."

We may classify the fundamental forms of nephritis as: (1) tubular nephritis; (23 glomerulo nephritis; (3) renal sclerosis.

It must always be remembered, however, in dealing with any classification of nephritis, that transitional forms are very frequent.

The clinical manifestations of the three broad types into which nephritis may be divided, are as follows:

1. *Tubular Nephritis.*—Very mild tubular nephritis occurs in a great many infectious diseases, and it is hardly worth while to attempt to separate those conditions which are merely toxic degenerations of the epithelium from those which are frankly inflammatory. The milder cases have few symptoms, in the more severe cases oliguria and anemia may occur. Edema is usually marked, but there is little tendency to uremia, nor is the blood pressure usually high. The urine contains a heavy trace of albumin with many casts.

2. *Glomerulonephritis.*—This form is likely to occur in connection with scarlet fever, or streptococcus infections. In the acute stages

15. Med. Clin. N. Am. **1**: 1918.

the symptoms are oliguria, with marked albuminuria and abundant casts, often considerable blood, high specific gravity of the urine, edema, moderate elevation of the blood pressure, and a tendency to uremia. The greater albuminuria, the microscopic findings in the urine, the higher blood pressure, and the tendency to uremia differentiate it from tubular nephritis.

In chronic glomerulonephritis the patient is pale and pasty looking, with digestive disturbances, coating of the tongue and general weakness, with circulatory disturbances. The blood pressure is high, often considerably over 200 mm., and there is usually distinct cardiac hypertrophy. There is usually polyuria, and a low gravity urine, usually rather definitely fixed between 1.011 and 1.013. An occasional examination of the urine may show neither albumin nor casts. Toxic symptoms significant of uremia appear sooner or later, and a large proportion of these patients die of uremia.

3. *Renal Sclerosis.*—This term means simply an end stage in some other form of renal disease. This may occur secondary to tubercular or glomerulonephritis or to widespread arterial disease involving the smaller arterioles of the kidney.

The following is a brief summary of the important features of the foregoing types:

1. Tubular Nephritis: (*a*). Mild, with practically no symptoms except albuminuria and cylindruria; is likely to occur in most acute infectious diseases; (*b*) severe, with characteristic urinary findings and edema.

2. Glomerulo Nephritis: (*a*). Acute form with dropsy, mild or severe hematuria, as well as a tendency to uremia; (*b*) subacute or intermediary form, with scarcely any renal symptoms, but with pronounced elevation of blood pressure; (*c*) chronic form, with excessive blood pressure, marked fixation of the specific gravity of the urine, tendency to uremia, disturbances of vision, and suggestive appearance of the patient.

3. Renal Sclerosis: (*a*) possibly primary renal sclerosis following acute interstitial nephritis; (*b*) secondary renal sclerosis following glomerulonephritis and mixed nephritis; (*c*) arteriolar nephritis or benign sclerosis, with high blood pressure, but with little impairment of renal function; (*d*) arteriosclerotic atrophy of the kidney.

Van Zant[16] calls especial attention to nephritis as a result of focal infection. Hemorrhage occurs into the glomerular capsule and tubules as a result of lesions in the glomerular capillaries, creating a hemorrhagic type of nephritis. It is believed by most investigators that bacteria from the primary focus plug up the glomerular capillaries.

16. Colorado Med., 1917, p. 325.

It is interesting and instructive to note that sometimes numbers of cases seem to spring up in a community in quick succession. This would seem to indicate the endemic presence from time to time of a form of streptococcus possessing a special affinity for the tonsils, and secondarily for the kidneys. It is not unlikely that many cases of so-called "idiopathic" acute nephritis, or nephritis from cold, may have an overlooked tonsillar origin (the reviewer wishes to emphasize this point, and believes it to be especially true as regards children). The great symptom of most of these cases is hematuria, not transient or mild, but pronounced in its degree, prolonged in its presence, and disproportionate to the other urinary features. Blood in the urine is often so abundant as to be visible macroscopically for several weeks. The nephritis does not ordinarily appear at the same time as the tonsillitis, but is more likely to show itself in from one to three weeks after the initial tonsillitis has subsided. The prognosis is usually good, and it is of great importance to remove the tonsils as soon as the acute throat symptoms have subsided.

Cross[17] reports four cases of nephritis following sore throat, and attaches especial importance to the streptococcus as a cause of renal disease. He believes that not enough attention is paid to the relation of acute infection of the nasopharynx to nephritis. With the causative organism incarcerated in the tonsillar crypts, buried in the nasopharyngeal tissue, or at the apex of a tooth, what is the mode of assault on the kidney? If we grant that it remains fixed in its *locus* and only its toxin circulates in the blood stream, exercising a special chemical affinity for the renal epithelium, we may think of an acute degeneration of the cells of the kidney tubules. Rather more likely is the probability that the process is one of hematogenous infection, bacterial emboli being carried direct to the kidney, and establishing a true glomerulonephritis. Kidney involvement may appear at any time during or after the local infection. The average period is from seven to fourteen days. The latent reserve power of the kidney is the most important consideration in prognosis. With a severe acute toxemia we may lose our patient; with a continual influence at work, the kidney condition may go on to a diffuse nephritis with permanent damage, anatomic and functional, with all that that implies. In most of the cases, however, the outlook is favorable. The offending tonsils should be removed, but not too early. It is usually best to wait for two or three weeks after the onset of the nephritis.

Butterworth[18] discusses syphilitic nephritis. Not infrequently there are seen in infancy and childhood cases of nephritis that can be

17. Long Island M. J. **12**:15, 1918.
18. Arch. Pediat., June, 1917.

explained in no other way than on a syphilitic basis. In one group of cases the clinical symptoms of nephritis may be wanting, and so insignificant as to pass unnoticed; repeated examinations of the urine may be necessary in order to make a diagnosis. If the child survives the early period of life, then the clinical manifestations are those commonly associated with a chronic interstitial nephritis. Fetal syphilis may result in various kidney changes, such as congenital malformations, cystic kidneys, etc., but the most common syphilitic manifestations may be classed as follows:

1. Acute parenchymatous nephritis, which may be hemorrhagic.
2. Acute interstitial nephritis.
3. Chronic interstitial nephritis.
4. Amyloid degeneration.
5. Gummas of the kidney.

Fowler's[19] classification of syphilitic nephropathies is as follows:

1. Secondary syphilis: (*a*) Transient albuminuria; (*b*) acute and subacute nephritis.

2. Tertiary stage: (*a*) Chronic interstitial and parenchymatous nephritis; (*b*) amyloid kidney; (*c*) gumma.

3. Hereditary syphilis: (*a*) early nephropathies; (*b*) late lesions.

In hereditary syphilis all varieties of nephritis are met with, but as a rule the kidney changes are overshadowed in importance by other manifestations of the disease. The kidney lesions may occur at two distinct periods: in early life, associated with other visceral lesions, and as a late complication. As a rule, there are few or no symptoms referable to the kidney. The pathologic changes most commonly found give rise to no symptoms aside from depressed renal function. These children are usually underdeveloped, undernourished and anemic. To the naked eye the kidney may appear normal, although under the microscope definite histologic changes may be seen. The kidney may show hyperemia and punctiform hemorrhages. Occasionally whitish or yellowish nodules are found in the deeper layers. They are composed for the most part of connective tissue, but may show caseous degeneration.

As regards prognosis, it is probable that many unrecognized cases are cured by antisyphilitic treatment. Fowler feels that the prognosis is not so bad as the literature would suggest.

MISCELLANEOUS

Rubow[20] remarks that the three main groups of medical kidney diseases are those due to epithelial degeneration, to glomerular

19. Med. and Surg., St. Louis **2**:54, 1918.

20. Hospitalstidende, **61**: No. 24, 1918; Quoted from Abstr. in J. A. M. A. **71**:695, 1918.

nephritis, and to sclerosis of the vessels in the kidney. The blood pressure is inclined to go up as soon as the glomeruli become involved. He warns that if the blood pressure naturally is low, as frequently happens in the young, there may be a considerable rise in the arterial pressure while it still is within apparently normal range. In certain cases the high blood pressure is almost the only certain sign of pathologic conditions in the glomeruli, and he queries whether from this alone, along with the following hypertrophy of the heart, we can draw the conclusion as to serious damage of the glomeruli and sclerosis of the vessels. Functional tests of the kidney may prove misleading with negative responses, as the normal range of functioning in human organs is so great. Healthy kidneys are capable of at least three times the work ordinarily imposed on them. This explains the long latent stage with chronic kidney disease, and shows that ordinary functional tests may give apparently normal findings for a long time even with encroaching disease. Only when the test is applied up to the maximal limit of normal functioning, can the findings be depended on to reveal slight degrees of functional deficiency, and therewith the beginning disease. It is difficult and possibly dangerous to apply a maximal test of this kind.

Even the determination of the residual nitrogen in the blood may prove misleading, if the residual nitrogen happens to be anchored in the solid tissues; in the liver, for example, and is not circulating in the blood. Some deny the possibility of this, but Monakow's research in 1914 on this historetention of residual nitrogen not only confirmed it but showed that the residual nitrogen in the blood is an unreliable index of the amount retained. He had a patient with reflex anuria for five days, and the fifth day the blood showed 50 mg. percentage of residual nitrogen in the blood, corresponding to about 3 gm. nitrogen. When the anuria stopped, it was found that there had been retention of 62 gm. nitrogen, in addition to 7.5 liters water. There must have been 55 gm. of nitrogen retained in the solid tissues; that is, the tissues were able to retain eighteen times as much as the blood. Determination of the residual nitrogen has proved useful in many ways, but it cannot be counted on to reveal incipient disease of the glomeruli. It is possible that applying the test in connection with maximal overburdening of kidney functioning may prove instructive. For example, one man of 53, with high blood pressure and hypertrophy of the heart, had residual nitrogen in the blood, in the morning, 34 mg. per cent., but twenty-four hours after intake of 20 gm. urea the figure was 62 mg. per cent. — a figure essentially higher than would be presented by a normal person under the same test. In a second case with apparently the same high pressure and enlarged heart,

twenty-four hours after the intake of 20 gm. urea, the blood showed a residual nitrogen content only at the upper limit of normal.

The same conditions are inherent in the determination of chlorids. Only with extreme degrees of renal insufficiency is the chlorid content of the blood very high; the surplus is anchored in the solid tissues. When the glomeruli are unable to eliminate as usual, the consequent retention of urea and salt acts as a stimulant to extra functioning on the part of the glomeruli still capable of functioning, as these substances have a diuretic action. Another means by which the organism seeks to compensate the deficient glomeruli is by sending the blood through the kidneys under greater pressure. The rise in blood pressure, and consequent hypertrophy of the heart, occurs early, and in many cases this alone answers the desired purpose of keeping renal elimination within practically normal range. The high blood pressure and hypertrophy of the heart, in combination with slight albuminuria, are therefore the bases for the diagnosis. Polycythemia may complicate kidney disease, and in the one typical case that has come to necropsy, chronic glomerular nephritis was found. The high blood pressure with kidney disease persists unmodified by repose in bed and dieting. The numerous transitional cases between glomerular nephritis and renal angiosclerosis show that there is no essential difference between them. The cardiovascular form may be regarded as a more or less protracted phase of a compensated stage of kidney sclerosis, while the uremic form is the stage of insufficiency when compensation is failing, or when from the first it has been inadequate. Death may occur from hemorrhage in the brain or from heart failure while the kidney trouble is still in the compensated phase. The findings in the kidney then will be quite different from those with death from uremia.

Meara[21] reports a case of unexplained high blood pressure in a boy 8½ years old. The systolic blood pressure was 210 mm., the diastolic 150. The boy appeared healthy and well, but had been subject to intense headaches ever since he was 5 years old. The heart was much enlarged, and the aortic second sound accentuated. There was a transitory edema of the legs, and the eye grounds showed arteriosclerosis of the retinal vessels, with some hemorrhagic exudate. The urine had a gravity of 1.010 and a trace of albumin, but no casts. The phenolsulphonephthalein test was 63 per cent., and the urea nitrogen of the blood 20 mg. per 100 c.c. blood, both within normal limits. The boy developed a severe hematuria, with intestinal hemorrhage, and finally died from mesenteric thrombosis.

This case corresponds exactly to the cases of "chronic interstitial nephritis" that have been reported before in children, with the excep-

21. Med. Clin. N. Am., July, 1918, p. 5.

tion of the fact that Meara's patient was a well developed, robust boy, who did not show the condition of the infantilism that usually goes with the condition. The etiology is unknown; the prognosis bad.

Foster[22] believes that there are three distinct and basic types of what is called "uremia." Clinically, it is rare to see one type uncomplicated by the others.

1. Simple retention of nitrogenous waste. A urinary poisoning, which occurs with complete anuria. In this type convulsions and other nervous symptoms are lacking. The essential positive symptoms are progressive asthenia and anorexia; later stupor and death.

2. The second type occurs with defective water and salt metabolism, resulting in cerebral edema. Convulsions are usually absent, and the blood pressure is not high. There is no marked nitrogen retention. At necropsy the conspicuous condition is edema, especially of the brain and meninges. The cerebrospinal fluid is under increased pressure, and after lumbar puncture there is temporary improvement.

3. The third, or convulsive type of uremia is due, Foster believes, to an abnormal catabolism. It is from such cases that he has isolated a very toxic crystalline substance which kills a guinea-pig with convulsions and coma. He believes that this is not a normal excretory product, but a product of abnormal metabolism.

Sailer[23] has investigated the composition of the sweat in nephritis. He admits that it was shown years ago by Austin and Miller that the blood nitrogen of a nephritic patient was not altered by sweating. But is it not possible that the urea in sweat is drawn from the tissues and not from the blood? Sailer investigated several cases with this in view, and found that usually the percentage of urea in the sweat of a nephritic was greater than that in his blood, which supports his hypothesis that the urea is drawn from the tissues.

Frissel and Vogel[23] discuss the value of the various renal function tests. The functional tests which are now being used may be divided into the following groups:

1. The determination of the rate of excretion in the urine of known amount of a chemical substance, injected or ingested.

2. Determination of the degree of retention in the blood of various normal metabolic products.

3. Comparison in a patient on a known test diet of the ingestion and excretion of nitrogen, salt and water.

4. A determination of the ratio between the concentration of various metabolic products (ordinarily urea) in the blood, and their excretion in the urine, the result being expressed as a ratio or coefficient of excretion.

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22. J. A. M. A. **67**:927, 1916.
23. Pennsylvania M. J. **21**:245, 1918.

Frissell and Vogel consider as abnormal a phenolsulphonephthalein excretion below 50 per cent. in two hours, a nonprotein nitrogen of the blood above 35 mg. per 100 c.c. of blood, or a urea nitrogen above 25 mg. per 100 c.c. blood.

They arrive at these conclusions:

1. Kidney function tests have a real prognostic value, particularly if the results are constantly abnormal on repeated examinations.

2. The higher values for the blood retention products are found mainly in the terminal stages of nephritis.

3. By plotting the curve of a very large series of cases it should be possible to arrive at an average expectation of life as indicated by any individual determination.

4. The value of diet and drugs may in the future be shown more clearly by these methods than by any other means now available.

Atchley[24] has made an intensive chemical study of eight cases of actue nephritis. A phenolsulphonephthalein excretion below 20 per cent. in acute nephritis is likely to carry with it a serious prognosis; higher value than this need not cause any worry. Urea retention was found in only three cases on admission. Three of the other patients showed no urea retention all the time that they were in the hospital. Two patients retained urea constantly even on a low salt and nitrogen intake. The highest figure for blood urea was in the only fatal case, the only other high urea was in the next most severe case. A high blood urea is probably of serious import in acute nephritis. Atchley doubts the value of the Ambard coefficient, and believes that even moderately rigid interpretation of it as a real index of the exact degree of impairment of urea function may lead to the gravest error. Edema was present in every one of the eight cases studied. While a patient was losing edema there was also a great sweeping out of salt and water; but after reaching a constant weight there is likely to be no abnormality of salt or of water function in the daily balances. It seems clear that the salt function is the first to be regained, followed at varying intervals by the pouring out of water with a coincident decrease in weight.

The first step in the treatment of acute nephritis should be the restriction of salt. The caloric requirement should be maintained from the very beginning, though it is wise to give a low protein intake to all cases of acute nephritis. When there is no retention of urea, 8 to 10 gm. of nitrogen (roughly 60 gm. protein) is a safe intake for an adult, but if there is nitrogen retention 6 gm. (roughly 40 gm. protein) should be the upper limit.

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24. Arch. Int. Med. **22**:56, 1918.

Frothingham[25] has made studies of renal function in various acute infectious diseases, such as pneumonia, rheumatic fever, typhoid, etc., and arrives at the following conclusions:

In the acute infections in which there is no clinical evidence of serious renal involvement, there is no constant impairment of renal function, as shown by the various functional tests, either during or after the acute stage of infection has passed. In some cases of infectious disease certain suggestions of impairment of function occur, but not constantly enough to draw any definite conclusions. The most striking thing in all groups studied was the frequency of an abnormally high index of urea excretion during the course of the fever. As this increase in the index was not associated with an increase in the phenolsulphonephthalein excretion or an abnormally low blood urea, in most of these cases it seems more likely that some factors peculiar to fever affect this test, rather than that the kidneys themselves are hyperactive during fever. It may be concluded that the various tests for kidney function failed to show any consistent evidence of impaired renal function during the course of or following these acute infections in which the clinical picture or the urinary examination by the older clinical methods showed nothing suggestive of renal damage.

Williams[26] believes that diuretics are useless in the treatment of nephritis. If a patient is dyspneic and edematous it is quite likely that he has a disturbance of salt metabolism. Such a patient should be given no other food than one quart of milk plus one pint of water daily for a week or two weeks (few authorities believe in restricting the diet as much as this, even in the most severe cases. L. W. H.). Later, starchy foods, and vegetables rich in iron and calcium may be added. Protein food is given according to the ability of the body to handle it. It is Williams' plan to put these cases on low diets, cautiously building them up as above suggested. At the same time a record is kept of the patient's muscular vigor by means of a dynamometer. As a result of the studies which have thus far been made, Williams feels that a patient gains in muscular vigor on a diet which his body can care for, even though it be much below his normal needs, and he will lose in muscular tone if he is fed ever so cautiously beyond his metabolic limitations. There is no value in persistent purgation with salts or in the use of hot packs.

As a summary, he concludes that kidney disease is probably a constitutional disease with kidney manifestations. In many cases the liability is commonly associated with nephritis and may bear a causal

25. Arch. Int. Med. **22**:74, 1918.
26. Med. Rec. **92**:624, 1917.

relationship to it. The best functional test for the general practitioner is the two-hour renal test.[27] Tests for albumin and casts are much less valuable. The phenolsulphonephthalein test is also extremely valuable. Blood studies for nonprotein nitrogen, urea, creatinin, and the determination of the Ambard-McLean coefficient are of considerable importance, but can be done only in a well equipped hospital laboratory. The Karrell (milk) diet is the best treatment for advanced cases with edema and dyspnea. Death is caused by acidosis (not always, certainly, L. W. H.) probably due to retention of phosphates. Calcium and iron both favor the elimination of phosphates and are the best medicines for the disease. Packs, purges and diuretics are probably of little value.

As regards prognosis, blood chemical studies furnish the most reliable evidence of the condition of the patient, and afford a better prognostic guide than does the two-hour renal test. The blood chemical methods are, however, too complex, and are far beyond the laboratory means of the general practitioner, and indeed the majority of hospitals. The two-hour renal test, on the contrary, is much simpler. Important and valuable parts of it can be done by the general practitioner without any technical training or laboratory experience. Merely measuring the urine excretion and determining its specific gravity every two hours during the day, and estimating the amount and gravity of the night urine, are extremely valuable guides in diagnosis, prognosis and treatment.[28]

PROGNOSIS

Christian[29] believes that functional tests have helped us a great deal in prognosis. Several of the methods yield results which are expressed numerically, and this makes it easy to compare results from time to time. It is of the utmost importance, however, to consider the patient as a whole, and not to place too much reliance on any one test or group of tests. Certain extrarenal factors may influence kidney tests a good deal; that is, severe anemia or cardiac decompensation. Under such conditions some functional tests may indicate advanced nephritis, and yet the kidneys may be really sound. Repeated tests are of the most value in prognosis, as we must know how rapidly any given condition is progressing. When renal function is fairly good, the chance for prognostic error is greatest. It may be said that there are two fairly distinct groups of nephritics as regards prognosis: (1) Progress slow and steady; (2) progression by sudden exacerbations.

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27. Mosenthal: Arch. Int. Med. **16**:733, 1915.
28. Hill, L. W.: Am. J. Dis. Child. **14**:267, 1917.
29. Pennsylvania M. J. **21**:233, 1918.

Four functional tests are used at the Peter Bent Brigham Hospital:

1. Phthalein test.
2. Blood urea and Ambard coefficient determinations.
3. Mosenthal test meal (called elsewhere "two-hour renal test").
4. The amount of diuresis produced by such a diuretic as theophyllin.

As a summary, Christian says that tests of renal function give us additional facts on which to base a prognosis as to renal lesions. "They will, if used with such limitations as are indicated above, greatly improve prognosis, but they will only reduce, not eliminate, our prognostic errors. Too many factors play a part in the humain organism to permit perfection in prognosis. Properly interpreted tests of renal function aid us much in the management of nephritic patients. Often they enable us to determine serious conditions not previously suspected. Frequently they enable us to bring to our patients a far more cheerful outlook than seemed justified from the data obtained by other methods of examining the patient."

99. Commonwealth Avenue.

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